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(54) Title: AZA- AND POLYAZA-NAPHTHALENYL CARBOXAMIDES USEFUL AS HIV INTEGRASE INHIBITORS

(57) Abstract: Aza- and polyaza-naphthalenyl carboxamide derivatives including certain quinoline carboxamide and naphthyridine carboxamide derivatives are described. These compounds are inhibitors of HIV integrase and inhibitors of HIV replication, and are useful in the prevention or treatment of infection by HIV and the treatment of AIDS, as compounds or pharmaceutically acceptable salts, or as ingredients in pharmaceutical compositions, optionally in combination with other antivirals, immunomodulators, antibiotics or vaccines. Methods of preventing, treating or delaying the onset of AIDS and methods of preventing or treating infection by HIV are also described.

TITLE OF THE INVENTION

AZA- AND POLYAZA-NAPHTHALENYL CARBOXAMIDES USEFUL AS HIV INTEGRASE INHIBITORS

FIELD OF THE INVENTION

The present invention is directed to aza- and polyaza-naphthalenyl carboxamides and pharmaceutically acceptable salts thereof, their synthesis, and their use as inhibitors of the HIV integrase enzyme. The compounds of the present invention include 7-(N-substituted carboxamido)-8-hydroxy- 1,6-naphthyridines and quinoxalines. The compounds and pharmaceutically acceptable salts thereof of the present invention are useful for preventing or treating infection by HIV and for treating AIDS.

References are made throughout this application to various published documents in order to more fully describe the state of the art to which this invention pertains. The disclosures of these references are hereby incorporated by reference in their entireties.

BACKGROUND OF THE INVENTION

A retrovirus designated human immunodeficiency virus (HIV) is the etiological agent of the complex disease that includes progressive destruction of the immune system (acquired immune deficiency syndrome; AIDS) and degeneration of the central and peripheral nervous system. This virus was previously known as LAV, HTLV-III, or ARV. A common feature of retrovirus replication is the insertion by virally-encoded integrase of proviral DNA into the host cell genome, a required step in HIV replication in human T-lymphoid and monocytoid cells. Integration is believed to be mediated by integrase in three steps: assembly of a stable nucleoprotein complex with viral DNA sequences; cleavage of two nucleotides from the 3' termini of the linear proviral DNA; covalent joining of the recessed 3' OH termini of the proviral DNA at a staggered cut made at the host target site. The fourth step in the process, repair synthesis of the resultant gap, may be accomplished by cellular enzymes.

Nucleotide sequencing of HIV shows the presence of a pol gene in one open reading frame [Ratner, L. et al., Nature, 313, 277(1985)]. Amino acid sequence homology provides evidence that the pol sequence encodes reverse

transcriptase, integrase and an HIV protease [Toh, H. et al., EMBO J. 4, 1267 (1985); Power, M.D. et al., Science, 231, 1567 (1986); Pearl, L.H. et al., Nature, 329, 351 (1987)]. All three enzymes have been shown to be essential for the replication of HIV.

It is known that some antiviral compounds which act as inhibitors of HIV replication are effective agents in the treatment of AIDS and similar diseases, including reverse transcriptase inhibitors such as azidothymidine (AZT) and efavirenz and protease inhbitors such as indinavir and nelfinavir. The compounds of this invention are inhibitors of HIV integrase and inhibitors of HIV replication. The inhibition of integrase in vitro and HIV replication in cells is a direct result of inhibiting the strand transfer reaction catalyzed by the recombinant integrase in vitro in HIV infected cells. The particular advantage of the present invention is highly specific inhibition of HIV integrase and HIV replication.

The following references are of interest as background:

Chemical Abstracts No. 33-2525 discloses the preparation of 5-chloro-8-hydroxy-1,6-naphthyridine-7-carboxylic acid amide from the corresponding methyl ester.

Derwent Abstract No. 97-048296 is an abstract of Japanse Published Application No. 08301849. The abstract discloses certain heterocyclic carboxamide derivatives. The derivatives are said to be useful as tachykinin receptor inhibitors. *N*-(3,5-bis(trifluoromethyl)benzyl-1,2-dihydro-*N*,2-dimethyl-1-oxo-4-pyrrolidino-3-isoquinoline carboxamide is specifically disclosed.

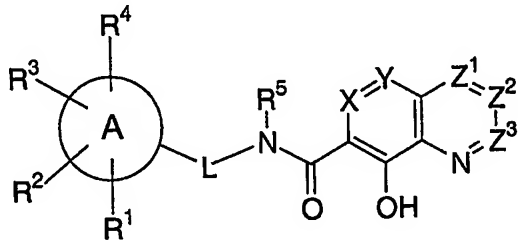
WO 98/13350 discloses certain quinoline derivatives which inhibit vascular endothelial growth factor. The reference also discloses certain 1,8-naphthryidine derivatives; i.e., Examples 53 and 54 respectively describe preparations of 2-acetamido-5-(2-fluoro-5-hydroxy-4-methylanilino)-1,8-naphthyridine and 2-amino-5-(2-fluoro-5-hydroxy-4-methylanilino)-1,8-naphthyridine.

WO 99/32450 discloses 4-hydroxyquinoline-2-carboxamide derivatives which are proposed for use in treating herpes virus infections.

WO 98/11073 discloses 8-hydroxyquinoline-7carboxamides which are proposed for use in treating herpes virus infections.

SUMMARY OF THE INVENTION

The present invention is directed to novel aza- and polyaza-naphthalenyl carboxamides. These compounds are useful in the inhibition of HIV integrase, the prevention of infection by HIV, the treatment of infection by HIV and in the prevention, treatment, and delay in the onset of AIDS and/or ARC, either as compounds or their pharmaceutically acceptable salts or hydrates (when appropriate), or as pharmaceutical composition ingredients, whether or not in combination with other HIV/AIDS antivirals, anti-infectives, immunomodulators, antibiotics or vaccines. More particularly, the present invention includes a compound of Formula (I):



(I),

wherein A is phenyl or phenyl fused to a carbocycle to form a fused carbocyclic ring system;

A is substituted by R^1, R^2, R^3, and R^4;

L is a linker connecting a ring atom of A to the nitrogen of the -N(R^5)- moiety, wherein L is

(i) a single bond,
(ii) -(C_{1-6} alkyl)-,
(iii) -(C_{2-6} alkenyl)-,
(iv) -(C_{0-6} alkyl)-(C_{3-6} cycloalkyl)-(C_{0-6} alkyl)-, or
(v) -(C_{0-6} alkyl)-M-(C_{0-6} alkyl)-, wherein M is -N(R^a)-, -OC(=O)-, or -C(=O)O-; wherein the alkenyl in (iii) and the alkyls in (ii), (iv), and (v) are independently and optionally substituted with 1, 2, or 3 substituents independently selected from the group consisting of halogen, -OH, -C_{1-6} alkyl, -O-C_{1-6} alkyl,

$-CO_2R^a$, $-CO_2(CH_2)_{1-2}R^k$, $-C_{1-6}$ alkyl-OR^a, $-R^k$, $-(CH_2)_{1-2}R^k$, $-CH(OR^a)-R^k$, and $-CH(N(R^a)_2)-R^k$;

X is N or C-Q^1;

Y is N or C-Q^2, provided that X and Y are not both N;

Z^1 is N or C-Q^3;

Z^2 is N or C-Q^4;

Z^3 is N or CH;

Q^1, Q^2, Q^3, and Q^4 are as defined in (i) or (ii) as follows:

(i) each of Q^1, Q^2, Q^3, and Q^4 is independently

(1) -H,
(2) $-C_{1-6}$ alkyl,
(3) $-C_{1-6}$ haloalkyl,
(4) $-O-C_{1-6}$ alkyl,
(5) $-O-C_{1-6}$ haloalkyl,
(6) halo,
(7) -CN,
(8) $-C_{1-6}$ alkyl-OR^a,
(9) $-C_{0-6}$ alkyl-$C(=O)R^a$,
(10) $-C_{0-6}$ alkyl-CO_2R^a,
(11) $-C_{0-6}$ alkyl-SR^a,
(12) $-N(R^a)_2$,
(13) $-C_{1-6}$ alkyl-$N(R^a)_2$,
(14) $-C_{0-6}$ alkyl-$C(=O)N(R^a)_2$,
(15) $-C_{0-6}$ alkyl-G-C_{1-6} alkyl-$C(=O)N(R^a)_2$, wherein G is O, S, $N(R^a)$, or $N(SO_2R^a)$,
(16) $-N(R^a)-C(R^a)=O$,
(17) $-C_{1-6}$ alkyl-$N(R^a)-C(R^a)=O$,

(18) -C(=O)-N(R^a)-C_{1-6} alkyl-[C(=O)]$_{0-1}$-N(R^a)$_2$,

(19) -C(=O)-N(R^a)-C_{1-6} alkyl substituted with 1 or 2 -OR^a,

(20) -C_{0-6} alkyl-SO_2R^a,

(21) -C_{0-6} alkyl-N(R^a)SO_2R^a,

(22) -C_{2-6} alkenyl,

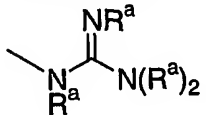
(23) -C_{2-6} alkenyl-C(=O)-N(R^a)$_2$,

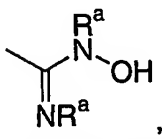
(24) -C_{2-5} alkynyl,

(25) -C_{2-5} alkynyl-CH_2N(R^a)$_2$,

(26) -C_{2-5} alkynyl-CH_2OR^a,

(27) -C_{2-5} alkynyl-$CH_2S(O)_n$-R^a, or

(28)  ,

(29)  ,

(30) -C(=NR^a)-N(R^a)$_2$,

(31) -N(R^a)-C_{1-6} alkyl-$S(O)_nR^a$,

(32) -N(R^a)-C_{1-6} alkyl-OR^a,

(33) -N(R^a)-C_{1-6} alkyl-N(R^a)$_2$,

(34) -N(R^a)-C_{1-6} alkyl-N(R^a)-C(R^a)=O,

(35) -N(R^a)-C_{0-6} alkyl-[C(=O)]$_{1-2}$N(R^a)$_2$,

(36) -N(R^a)-C_{1-6} alkyl-CO_2R^a,

(37) -N(R^a)C(=O)N(R^a)-C_{1-6} alkyl-C(=O)N(R^a)$_2$,

(38) -N(R^a)C(=O)-C_{1-6} alkyl-N(R^a)$_2$,

(39) -N(R^a)-SO_2-N(R^a)$_2$,

(40) -R^k,

(41) -C_{1-6} alkyl substituted with R^k,

(42) -C_{1-6} haloalkyl substituted with R^k,

(43) -C_{2-5} alkenyl-R^k,

(44) -C_{2-5} alkynyl-R^k,

(45) -C_{0-6} alkyl-O-R^k,

(46) -C_{0-6} alkyl-O-C_{1-6} alkyl-R^k,

(47) -C_{0-6} alkyl-$S(O)_n$-R^k,

(48) -C_{0-6} alkyl-$S(O)_n$-C_{1-6} alkyl-R^k,
(49) -O-C_{1-6} alkyl-OR^k,
(50) -O-C_{1-6} alkyl-O-C_{1-6} alkyl-R^k,
(51) -O-C_{1-6} alkyl-$S(O)_nR^k$,
(52) -C_{0-6} alkyl-$N(R^c)$-R^k,
(53) -C_{0-6} alkyl-$N(R^c)$-C_{1-6} alkyl substituted with one or two R^k groups,
(54) -C_{0-6} alkyl-$N(R^c)$-C_{1-6} alkyl-OR^k,
(55) -C_{0-6} alkyl-C(=O)-R^k,
(56) -C_{0-6} alkyl-$C(=O)N(R^a)$-R^k,
(57) -C_{0-6} alkyl-$N(R^a)C(=O)$-R^k,
(58) -C_{0-6} alkyl-$C(=O)N(R^a)$-C_{1-6} alkyl-R^k, or
(59) -C_{0-6} alkyl-$N(R^a)$-C_{0-6} alkyl-$S(O)_nR^k$;

(ii) alternatively, Q^2 and Q^3 together with the carbon atoms to which they are attached and the fused ring carbon atom attached therebetween form a 5- or 6-membered monocyclic carbocycle or a 5- or 6-membered monocyclic heterocycle, wherein the heterocycle contains 1 or 2 heteroatoms selected from nitrogen, oxygen and sulfur, and wherein either the carbocycle or heterocycle is optionally substituted with from 1 to 3 substituents independently selected from

(1) -C_{1-6} alkyl,
(3) -C_{1-6} haloalkyl,
(4) -O-C_{1-6} alkyl,
(5) -O-C_{1-6} haloalkyl,
(6) halo,
(7) -CN,
(8) -C_{1-6} alkyl-OR^a,
(9) -C_{1-6} alkyl-$S(O)_nR^a$,
(10) -C_{1-6} alkyl-$N(R^a)_2$,
(11) -C_{1-6} alkyl-$C(=O)$-$N(R^a)_2$,
(12) -C_{1-6} alkyl-CO_2R^a,
(13) oxo,
(14) -R^k, and
(15) -C_{1-6} alkyl substituted with R^k; and

Q^1 and Q^4 are independently as defined in (i) above;

each of R^1 and R^2 is independently:

(1) -H,
(2) -C_{1-6} alkyl,
(3) -C_{1-6} haloalkyl,
(4) -O-C_{1-6} alkyl,
(5) -O-C_{1-6} haloalkyl,
(6) -OH
(7) halo,
(8) -NO_2,
(9) -CN,
(10) -C_{1-6} alkyl-OR^a,
(11) -C_{0-6} alkyl-$C(=O)R^a$,
(12) -C_{0-6} alkyl-CO_2R^a,
(13) -C_{0-6} alkyl-SR^a,
(14) -$N(R^a)_2$,
(15) -C_{1-6} alkyl-$N(R^a)_2$,
(16) -C_{0-6} alkyl-$C(=O)N(R^a)_2$,
(17) -C_{1-6} alkyl-$N(R^a)$-$C(R^a)=O$,
(18) -SO_2R^a,
(19) -$N(R^a)SO_2R^a$,
(20) -C_{2-5} alkenyl,
(21) -O-C_{1-6} alkyl-OR^a,
(22) -O-C_{1-6} alkyl-SR^a,
(23) -O-C_{1-6} alkyl-NH-CO_2R^a,
(24) -O-C_{2-6} alkyl-$N(R^a)_2$,
(25) -$N(R^a)$-C_{1-6} alkyl-SR^a,
(26) -$N(R^a)$-C_{1-6} alkyl-OR^a,
(27) -$N(R^a)$-C_{1-6} alkyl-$N(R^a)_2$,
(28) -$N(R^a)$-C_{1-6} alkyl-$N(R^a)$-$C(R^a)=O$,
(29) -R^k,
(30) -C_{1-6} alkyl substituted with 1 or 2 R^k groups,

(31) -C_{1-6} haloalkyl substituted with 1 or 2 R^k groups,
(32) -C_{2-5} alkenyl-R^k,
(33) -C_{2-5} alkynyl-R^k,
(34) -O-R^k,
(35) -O-C_{1-6} alkyl-R^k,
(36) -$S(O)_n$-R^k,
(37) -$S(O)_n$-C_{1-6} alkyl-R^k,
(38) -O-C_{1-6} alkyl-OR^k,
(39) -O-C_{1-6} alkyl-O-C_{1-6} alkyl-R^k,
(40) -O-C_{1-6} alkyl-$S(O)_nR^k$,
(41) -C_{1-6} alkyl (OR^b)(R^k),
(42) -C_{1-6} alkyl (OR^b)(-C_{1-6} alkyl-R^k),
(43) -C_{0-6} alkyl-$N(R^b)(R^k)$,
(44) -C_{0-6} alkyl-$N(R^b)$(-C_{1-6} alkyl-R^k),
(45) -C_{1-6} alkyl $S(O)_n$-R^k,
(46) -C_{1-6} alkyl $S(O)_n$-C_{1-6} alkyl-R^k,
(47) -C_{0-6} alkyl C(O)-R^k, or
(48) -C_{0-6} alkyl C(O)-C_{1-6} alkyl-R^k,

each of R^3 and R^4 is independently
(1) -H,
(2) halo,
(3) -CN,
(4) -NO_2,
(5) -OH,
(6) C_{1-6} alkyl,
(7) C_{1-6} haloalkyl,
(8) -O-C_{1-6} alkyl,
(9) -O-C_{1-6} haloalkyl,
(10) -C_{1-6} alkyl-OR^a,
(11) -C_{0-6} alkyl-C(=O)R^a,
(12) -C_{0-6} alkyl-CO_2R^a,
(13) -C_{0-6} alkyl-SR^a,
(14) -$N(R^a)_2$,

(15) -C_{1-6} alkyl-$N(R^a)_2$,
(16) -C_{0-6} alkyl-$C(=O)N(R^a)_2$,
(17) -SO_2R^a,
(18) -$N(R^a)SO_2R^a$,
(19) -C_{2-5} alkenyl,
(20) -O-C_{1-6} alkyl-OR^a,
(21) -O-C_{1-6} alkyl-SR^a,
(22) -O-C_{1-6} alkyl-NH-CO_2R^a, or
(23) -O-C_{2-6} alkyl-$N(R^a)_2$;

R^5 is

(1) -H,
(2) -C_{1-6} alkyl, optionally substituted with from 1 to 5 substituents independently selected from halogen, -O-C_{1-6} alkyl, -O-C_{1-6} haloalkyl, -$N(R^a)_2$, and -CO_2R^a;
(3) aryl optionally substituted with from 1 to 5 substituents independently selected from halogen, C_{1-6} alkyl, C_{1-6} haloalkyl, -O-C_{1-6} alkyl, -O-C_{1-6} haloalkyl, -S-C_{1-6} alkyl, -CN, and -OH, or
(4) -C_{1-6} alkyl substituted with R^k;

each R^a is independently -H, -C_{1-6} alkyl, or -C_{1-6} haloalkyl;

each R^b is independently:

(1) -H,
(2) -C_{1-4} alkyl,
(3) -C_{1-4} haloalkyl,
(4) -R^k,
(5) -C_{2-3} alkenyl,
(6) -C_{1-4} alkyl-R^k,
(7) -C_{2-3} alkenyl-R^k,
(8) -$S(O)_n$-R^k, or
(9) -C(O)-R^k;

each R^c is independently

(1) -H,
(2) -C_{1-6} alkyl,
(3) -C_{1-6} alkyl substituted with -$N(R^a)_2$, or
(4) -C_{1-4} alkyl-aryl, wherein aryl is optionally substituted with 1 to 5 substituents independently selected from halogen, C_{1-6} alkyl, C_{1-6} haloalkyl, -O-C_{1-6} alkyl, -O-C_{1-6} haloalkyl, -S-C_{1-6} alkyl, -CN, and -OH;

each R^k is independently carbocycle or heterocycle, wherein the carbocycle and heterocycle are unsubstituted or substituted with from 1 to 5 substituents each of which is independently selected from

(a) halogen,
(b) -C_{1-6} alkyl,
(c) -C_{1-6} haloalkyl,
(d) -O-C_{1-6} alkyl,
(e) -O-C_{1-6} haloalkyl,
(f) -S-C_{1-6} alkyl,
(g) -CN,
(h) -OH,
(i) oxo,
(j) -C_{0-6} alkyl-$C(=O)N(R^a)_2$,
(k) -C_{0-6} alkyl-$C(=O)R^a$,
(l) -$N(R^a)$-$C(=O)R^a$,
(m) -$N(R^a)$-CO_2R^a,
(n) -C_{1-6} alkyl-$N(R^a)$-$C(=O)R^a$,
(o) -$N(R^a)_2$,
(p) -C_{1-6} alkyl-$N(R^a)_2$,
(q) -C_{1-6} alkyl-OR^a,
(r) -C_{0-6} alkyl-CO_2R^a,
(s) -C_{0-6} alkyl-O-C_{1-6} alkyl-OR^a,
(t) -SO_2R^a,
(u) -$SO_2N(R^a)_2$,
(v) -C_{0-6} alkyl-CO_2-C_{2-5} alkenyl,

(w) aryl,
(x) aryloxy-,
(y) -C_{1-4} alkyl substituted with aryl,
(z) heteromonocycle,
(aa) -C_{1-4} alkyl substituted with a heteromonocycle,
(bb) heteromonocyclylcarbonyl-C_{0-6} alkyl-, and
(cc) N-heteromonocyclyl-N-C_{1-6} alkyl-amino-;

wherein the aryl group in (w) aryl, (x) aryloxy, and (y) -C_{1-4} alkyl substituted with aryl, is optionally substituted with from 1 to 4 substituents independently selected from halogen, C_{1-6} alkyl, -O-C_{1-6} alkyl, C_{1-6} alkyl substituted with $N(R^a)_2$, C_{1-6} haloalkyl, and -OH; and

wherein the heteromonocyclyl group in (z) heteromonocycle, (aa) -C_{1-4} alkyl substituted with a heteromonocycle, (bb) heteromonocyclyl-carbonyl-C_{0-6} alkyl-, and (cc) N-heteromonocyclyl-N-C_{1-6} alkyl-amino- is optionally substituted with from 1 to 4 substituents independently selected from halogen, C_{1-6} alkyl, -O-C_{1-6} alkyl, C_{1-6} haloalkyl, oxo, and -OH; and

each n is independently an integer equal to 0, 1 or 2;

and with the proviso that when Z^1 is C-Q^3, Z^2 is C-Q^4, Z^3 is CH, and X is C-Q^1, then Y is not C-Q^2;

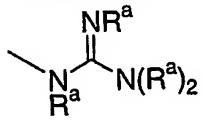
or a pharmaceutically acceptable salt thereof.

An aspect of the invention is a compound of Formula (I) as just defined above, except that part (i) of the definition of Q^1, Q^2, Q^3, and Q^4 does not include (59) -C_{0-6} alkyl-$N(R^a)$-C_{0-6} alkyl-$S(O)_nR^k$.

A first embodiment of the invention is a compound of Formula (I), wherein

each of Q^1, Q^2, Q^3, and Q^4 is independently

(1) -H,
(2) -C_{1-6} alkyl,
(3) -C_{1-6} fluoroalkyl,
(4) -O-C_{1-6} alkyl,
(5) -O-C_{1-6} fluoroalkyl,
(6) halo,
(7) -CN,
(8) -C_{1-6} alkyl-OR^a,
(9) -C_{0-6} alkyl-$C(=O)R^a$,
(10) -C_{0-6} alkyl-CO_2R^a,
(11) -C_{0-6} alkyl-SR^a,
(12) -$N(R^a)_2$,
(13) -C_{1-6} alkyl -$N(R^a)_2$,
(14) -C_{0-6} alkyl-$C(=O)N(R^a)_2$,
(15) -C_{1-6} alkyl-$N(R^a)$-$C(R^a)=O$,
(16) -SO_2R^a,
(17) -$N(R^a)SO_2R^a$,
(18) -C_{2-5} alkynyl,
(19) -C_{2-5} alkynyl-$CH_2N(R^a)_2$,
(20) -C_{2-5} alkynyl-CH_2OR^a,

(21)  ,

(22) -$N(R^a)$-C_{1-6} alkyl-SR^a,
(23) -$N(R^a)$-C_{1-6} alkyl-OR^a,
(24) -$N(R^a)$-C_{1-6} alkyl-$N(R^a)_2$,
(25) -$N(R^a)$-C_{1-6} alkyl-$N(R^a)$-$C(R^a)=O$,
(26) -R^k,
(27) -C_{1-6} alkyl substituted with R^k,
(28) -C_{1-6} fluoroalkyl substituted with R^k,
(29) -C_{2-5} alkenyl-R^k,
(30) -C_{2-5} alkynyl-R^k,
(31) -O-R^k,
(32) -O-C_{1-4} alkyl-R^k,

(33) $-S(O)_n-R^k$,
(34) $-S(O)_n-C_{1-4}$ alkyl-R^k,
(35) $-O-C_{1-6}$ alkyl-OR^k,
(36) $-O-C_{1-6}$ alkyl-$O-C_{1-4}$ alkyl-R^k,
(37) $-O-C_{1-6}$ alkyl-SR^k,
(38) $-N(R^c)-R^k$,
(39) $-N(R^c)-C_{1-6}$ alkyl substituted with one or two R^k groups,
(40) $-N(R^c)-C_{1-6}$ alkyl-OR^k,
(41) $-C(=O)N(R^a)-C_{1-6}$ alkyl-R^k,
(42) $-C_{2-5}$ alkynyl-$CH_2S(O)_n-R^a$, or
(43) $-C(=NR^a)-N(R^a)_2$;

each of R^1 and R^2 is independently:

(1) -H,
(2) $-C_{1-6}$ alkyl,
(3) $-C_{1-6}$ fluoroalkyl,
(4) $-O-C_{1-6}$ alkyl,
(5) $-O-C_{1-6}$ fluoroalkyl,
(6) -OH
(7) halo,
(8) $-NO_2$,
(9) -CN,
(10) $-C_{1-6}$ alkyl-OR^a,
(11) $-C_{0-6}$ alkyl-$C(=O)R^a$,
(12) $-C_{0-6}$ alkyl-CO_2R^a,
(13) $-C_{0-6}$ alkyl-SR^a,
(14) $-N(R^a)_2$,
(15) $-C_{1-6}$ alkyl-$N(R^a)_2$,
(16) $-C_{0-6}$ alkyl-$C(=O)N(R^a)_2$,
(17) $-C_{1-6}$ alkyl-$N(R^a)-C(R^a)=O$,
(18) $-SO_2R^a$,
(19) $-N(R^a)SO_2R^a$,
(20) $-C_{2-5}$ alkenyl,
(21) $-O-C_{1-6}$ alkyl-OR^a,

(22) -O-C_{1-6} alkyl-SR^a,
(23) -O-C_{1-6} alkyl-NH-CO_2R^a,
(24) -O-C_{2-6} alkyl-$N(R^a)_2$,
(25) -$N(R^a)$-C_{1-6} alkyl-SR^a,
(26) -$N(R^a)$-C_{1-6} alkyl-OR^a,
(27) -$N(R^a)$-C_{1-6} alkyl-$N(R^a)_2$,
(28) -$N(R^a)$-C_{1-6} alkyl-$N(R^a)$-$C(R^a)$=O,
(29) -R^k,
(30) -C_{1-6} alkyl substituted with 1 or 2 R^k groups,
(31) -C_{1-6} fluoroalkyl substituted with 1 or 2 R^k groups,
(32) -C_{2-5} alkenyl-R^k,
(33) -C_{2-5} alkynyl-R^k,
(34) -O-R^k,
(35) -O-C_{1-4} alkyl-R^k,
(36) -$S(O)_n$-R^k,
(37) -$S(O)_n$-C_{1-4} alkyl-R^k,
(38) -O-C_{1-6} alkyl-OR^k,
(39) -O-C_{1-6} alkyl-O-C_{1-4} alkyl-R^k,
(40) -O-C_{1-6} alkyl-SR^k,
(41) -C_{1-6} alkyl $(OR^b)(R^k)$,
(42) -C_{1-6} alkyl (OR^b)(-C_{1-4} alkyl-R^k),
(43) -C_{0-6} alkyl-$N(R^b)(R^k)$,
(44) -C_{0-6} alkyl-$N(R^b)$(-C_{1-4} alkyl-R^k),
(45) -C_{1-6} alkyl $S(O)_n$-R^k,
(46) -C_{1-6} alkyl $S(O)_n$-C_{1-4} alkyl-R^k,
(47) -C_{0-6} alkyl C(O)-R^k, or
(48) -C_{0-6} alkyl C(O)-C_{1-4} alkyl-R^k,

each of R^3 and R^4 is independently

(1) -H,
(2) halo,
(3) -CN,
(4) -NO_2,
(5) -OH,

(6) C_{1-6} alkyl,
(7) C_{1-6} fluoroalkyl,
(8) -O-C_{1-6} alkyl,
(9) -O-C_{1-6} fluoroalkyl,
(10) -C_{1-6} alkyl-OR^a,
(11) -C_{0-6} alkyl-C(=O)R^a,
(12) -C_{0-6} alkyl-CO_2R^a,
(13) -C_{0-6} alkyl-SR^a,
(14) -$N(R^a)_2$,
(15) -C_{1-6} alkyl-$N(R^a)_2$,
(16) -C_{0-6} alkyl-C(=O)$N(R^a)_2$,
(17) -SO_2R^a,
(18) -$N(R^a)SO_2R^a$,
(19) -C_{2-5} alkenyl,
(20) -O-C_{1-6} alkyl-OR^a,
(21) -O-C_{1-6} alkyl-SR^a,
(22) -O-C_{1-6} alkyl-NH-CO_2R^a, or
(23) -O-C_{2-6} alkyl-$N(R^a)_2$;

R^5 is

(1) -H,
(2) -C_{1-6} alkyl, optionally substituted with from 1 to 3 substituents independently selected from halogen, -O-C_{1-6} alkyl, -O-C_{1-6} fluoroalkyl, -$N(R^a)_2$, and -CO_2R^a;
(3) aryl optionally substituted with from 1 to 5 substituents independently selected from halogen, C_{1-6} alkyl, C_{1-6} fluoroalkyl, -O-C_{1-6} alkyl, -O-C_{1-6} fluoroalkyl, -S-C_{1-6} alkyl, -CN, and -OH, or
(4) -C_{1-6} alkyl substituted with R^k;

each R^a is independently -H, -C_{1-6} alkyl, or -C_{1-6} fluoroalkyl;

each R^b is independently:

(1) -H,

(2) -C_{1-4} alkyl,
(3) -C_{1-4} fluoroalkyl,
(4) -R^k,
(5) -C_{2-3} alkenyl,
(6) -C_{1-4} alkyl-R^k,
(7) -C_{2-3} alkenyl-R^k,
(8) -$S(O)_n$-R^k, or
(9) -C(O)-R^k;

each R^c is independently
(1) -H,
(2) -C_{1-6} alkyl,
(3) -C_{1-6} alkyl substituted with -$N(R^a)_2$, or
(4) -C_{1-4} alkyl-aryl, wherein aryl is optionally substituted with 1 to 5 substituents independently selected from halogen, C_{1-6} alkyl, C_{1-6} fluoroalkyl, -O-C_{1-6} alkyl, -O-C_{1-6} fluoroalkyl, -S-C_{1-6} alkyl, -CN, and -OH; and

each R^k is independently carbocycle or heterocycle, wherein the carbocycle and heterocycle are unsubstituted or substituted with from 1 to 5 substituents each of which is independently selected from
(a) halogen,
(b) C_{1-6} alkyl,
(c) C_{1-6} fluoroalkyl,
(d) -O-C_{1-6} alkyl,
(e) -O-C_{1-6} fluoroalkyl,
(f) -S-C_{1-6} alkyl,
(g) -CN,
(h) -OH,
(i) oxo,
(j) -$(CH_2)_{0-3}C(=O)N(R^a)_2$,
(k) -$(CH_2)_{0-3}C(=O)R^a$,
(l) -$N(R^a)$-$C(=O)R^a$,
(m) -$N(R^a)$-$C(=O)OR^a$,

(n) $-(CH_2)_{1-3}N(R^a)-C(=O)R^a$,
(o) $-N(R^a)_2$,
(p) $-C_{1-6}$ alkyl-$N(R^a)_2$,
(q) aryl,
(r) aryloxy-,
(s) $-C_{1-4}$ alkyl substituted with aryl,
(t) heteromonocycle,
(u) $-C_{1-4}$ alkyl substituted with a heteromonocycle,
(v) heteromonocyclylcarbonyl-C_{0-6} alkyl-, and
(w) N-heteromonocyclyl-N-C_{1-6} alkyl-amino-;

wherein the aryl group in (q) aryl, (r) aryloxy, and (s) $-C_{1-4}$ alkyl substituted with aryl, is optionally substituted with from 1 to 3 substituents independently selected from halogen, C_{1-6} alkyl, -O-C_{1-6} alkyl, C_{1-6} alkyl substituted with $N(R^a)_2$, C_{1-6} fluoroalkyl, and -OH; and

wherein the heteromonocyclyl group in (t) heteromonocycle, (u) $-C_{1-4}$ alkyl substituted with a heteromonocycle, (v) heteromonocyclyl-carbonyl-C_{0-6} alkyl-, and (w) N-heteromonocyclyl-N-C_{1-6} alkyl-amino- is optionally substituted with from 1 to 3 substituents independently selected from halogen, C_{1-6} alkyl, -O-C_{1-6} alkyl, C_{1-6} fluoroalkyl, oxo, and -OH;

and all other variables are as originally defined;

and with the proviso that when Z^1 is C-Q^3, Z^2 is C-Q^4, Z^3 is CH, and X is C-Q^1, then Y is not C-Q^2;

or a pharmaceutically acceptable salt thereof.

The present invention also includes pharmaceutical compositions containing a compound of the present invention and methods of preparing such pharmaceutical compositions. The present invention further includes methods of treating AIDS, methods of delaying the onset of AIDS, methods of preventing AIDS, methods of preventing infection by HIV, and methods of treating infection by HIV.

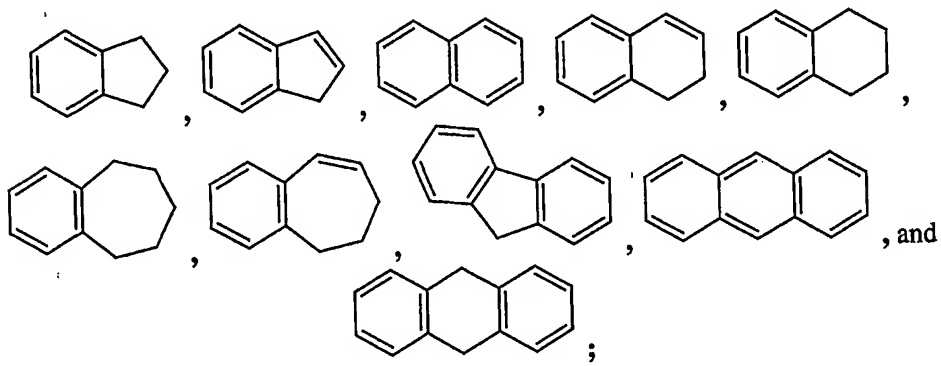
Other embodiments, aspects and features of the present invention are either further described in or will be apparent from the ensuing description, examples and appended claims.

DETAILED DESCRIPTION OF THE INVENTION

The present invention includes the aza- and polyaza-naphthalenyl carboxamides of Formula (I) above. These compounds and pharmaceutically acceptable salts thereof are HIV integrase inhibitors.

A second embodiment of the invention is a compound of Formula (I), wherein

A is phenyl or a fused carbocyclic ring system selected from the group consisting of



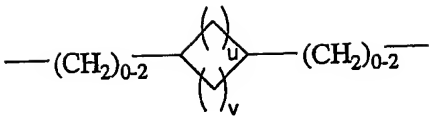
L is

(i) a single bond;

(ii) $-(CH_2)_{1-5}-$, which is optionally substituted with 1 or 2 substituents independently selected from the group consisting of halogen, -OH, $-C_{1-6}$ alkyl, $-O-C_{1-6}$ alkyl, $-CO_2R^a$, $-CO_2(CH_2)_{1-2}R^k$, $-C_{1-6}$ alkyl-OR^a, $-R^k$, $-(CH_2)_{1-2}R^k$, $-CH(OR^a)-R^k$, and $-CH(N(R^a)_2)-R^k$;

(iii) $-(CH_2)_{0-2}-CH=CH-(CH_2)_{1-2}-$, which is optionally substituted with 1, 2 or 3 substituents independently selected from the group consisting of halogen, -OH, $-C_{1-6}$ alkyl, and $-O-C_{1-6}$ alkyl;

(iv)



, wherein u and v are each integers having a value from 0 to 4, provided that the sum of u + v is 1, 2, 3 or 4;

or

(v) a heteroatom-containing chain which is $-(CH_2)_{0-3}N(R^a)-(CH_2)_{1-3}-$, $-(CH_2)_{1-2}-OC(=O)-(CH_2)_{1-2}-$, or $-(CH_2)_{1-2}-C(=O)O-(CH_2)_{1-2}-$;

R^5 is

(1) -H,

(2) $-C_{1-4}$ alkyl, optionally substituted with from 1 to 5 substituents independently selected from halogen, $-O-C_{1-6}$ alkyl, $-O-C_{1-6}$ haloalkyl, $-N(R^a)_2$, and $-CO_2R^a$;

(3) phenyl optionally substituted with from 1 to 5 substituents independently selected from halogen, C_{1-6} alkyl, C_{1-6} haloalkyl, $-O-C_{1-6}$ alkyl, $-O-C_{1-6}$ haloalkyl, $-S-C_{1-6}$ alkyl, -CN, and -OH, or

(4) $-C_{1-4}$ alkyl substituted with R^k;

each R^a is independently -H or $-C_{1-6}$ alkyl;

each R^c is independently

(1) -H,

(2) $-C_{1-4}$ alkyl,

(3) $-C_{1-4}$ alkyl substituted with $-N(R^a)_2$, or

(4) $-C_{1-4}$ alkyl-phenyl, wherein the phenyl is optionally substituted with 1 to 5 substituents independently selected from halogen, C_{1-6} alkyl, C_{1-6} haloalkyl, $-O-C_{1-6}$ alkyl, $-O-C_{1-6}$ haloalkyl, $-S-C_{1-6}$ alkyl, -CN, and -OH;

each R^k is independently:

(1) aryl selected from phenyl and naphthyl, wherein aryl is unsubstituted or substituted with from 1 to 5 substituents independently selected from:

(a) halogen,
(b) C_{1-6} alkyl,
(c) C_{1-6} haloalkyl,
(d) -O-C_{1-6} alkyl,
(e) -O-C_{1-6} haloalkyl,
(f) phenyl,
(g) -S-C_{1-6} alkyl,
(h) -CN,
(i) -OH,
(j) phenyloxy, unsubstituted or substituted with from 1 to 3 substituents independently selected from:
(i) halogen,
(ii) C_{1-6} alkyl,
(iii) C_{1-6} haloalkyl, and
(iv) -OH,
(k) $-N(R^a)_2$,
(l) -C_{1-6} alkyl-$N(R^a)_2$,
(m) $-R^t$,
(p) $-(CH_2)_{0-3}C(=O)N(R^a)_2$, and
(q) $-(CH_2)_{0-3}C(=O)R^a$;

(2) -C_{3-7} cycloalkyl, unsubstituted or substituted with from 1 to 3 substituents independently selected from:
(a) halogen,
(b) C_{1-6} alkyl,
(c) -O-C_{1-6} alkyl,
(d) C_{1-6} haloalkyl,
(e) -O-C_{1-6} haloalkyl,
(f) -CN,
(h) phenyl, and
(j) -OH;

(3) -C_{3-7} cycloalkyl fused with a phenyl ring, unsubstituted or substituted with from 1 to 5 substituents independently selected from:
(a) halogen,
(b) C_{1-6} alkyl,

(c) -O-C_{1-6} alkyl,
(d) C_{1-6} haloalkyl,
(e) -O-C_{1-6} haloalkyl,
(f) -CN, and
(g) -OH;

(4) a 5- or 6- membered heteroaromatic ring containing from 1 to 4 heteroatoms independently selected from oxygen, nitrogen and sulfur, wherein the heteroaromatic ring is unsubstituted or substituted on nitrogen or carbon with from 1 to 5 substituents independently selected from:

(a) halogen,
(b) C_{1-6} alkyl,
(c) C_{1-6} haloalkyl,
(d) -O-C_{1-6} alkyl,
(e) -O-C_{1-6} haloalkyl,
(f) phenyl,
(g) -S-C_{1-6} alkyl,
(h) -CN,
(i) -OH,
(j) phenyloxy, unsubstituted or substituted with from 1 to 3 substituents independently selected from:
(i) halogen,
(ii) C_{1-6} alkyl,
(iii) C_{1-6} haloalkyl, and
(iv) -OH,
(k) -$N(R^a)_2$,
(l) -C_{1-6} alkyl-$N(R^a)_2$,
(m) -R^t,
(n) oxo,
(o) -$(CH_2)_{0-3}C(=O)N(R^a)_2$, and
(p) -$(CH_2)_{0-3}C(=O)R^a$;

(5) a 5- or 6- or 7- or 8-membered heterocyclic ring selected from a saturated heterocyclic ring and a mono- or poly-unsaturated non-aromatic heterocyclic ring, wherein the heterocyclic ring contains from 1 to 4 heteroatoms independently selected from oxygen, nitrogen and sulfur, and wherein the

heterocyclic ring is unsubstituted or substituted with from 1 to 5 substituents independently selected from:

(a) halogen,
(b) C_{1-6} alkyl,
(c) -O-C_{1-6} alkyl,
(d) C_{1-6} haloalkyl,
(e) -O-C_{1-6} haloalkyl,
(f) -CN,
(g) oxo,
(h) phenyl
(i) benzyl,
(j) phenylethyl,
(k) -OH,
(l) $-(CH_2)_{0-3}C(=O)N(R^a)_2$,
(m) $-(CH_2)_{0-3}C(=O)R^a$,
(n) $-N(R^a)-C(=O)R^a$,
(o) $-N(R^a)-CO_2R^a$,
(p) $-(CH_2)_{1-3}N(R^a)-C(=O)R^a$,
(q) $-N(R^a)_2$,
(r) $-(CH_2)_{1-3}N(R^a)_2$,
(s) $-(CH_2)_{1-3}-OR^a$,
(t) $-(CH_2)_{0-3}CO_2R^a$,
(u) $-(CH_2)_{0-3}-O-(CH_2)_{1-3}-OR^a$,
(v) $-SO_2R^a$,
(w) $-SO_2N(R^a)_2$,
(x) $-(CH_2)_{0-3}C(=O)O(CH_2)_{1-2}CH=CH_2$,
(y) $-R^t$,
(z) $-(CH_2)_{0-3}C(=O)R^t$,
(aa) $-N(R^a)R^t$, and
(bb) $-(CH_2)_{1-3}R^t$; or

(6) an 8- to 10- membered heterobicyclic ring containing from 1 to 4 heteroatoms independently selected from oxygen, nitrogen and sulfur, wherein the heterobicyclic ring is saturated or unsaturated and is unsubstituted or substituted with from 1 to 5 substituents independently selected from:

(a) halogen,
(b) C_{1-6} alkyl,
(c) -O-C_{1-6} alkyl,
(d) C_{1-6} haloalkyl,
(e) -O-C_{1-6} haloalkyl,
(f) -CN,
(g) =O, and
(h) -OH; and

R^t is naphthyl or a 5- or 6-membered heteromonocylic ring containing from 1 to 4 nitrogen atoms, wherein the heteromonocyclic ring is saturated or unsaturated, and wherein either the naphthyl or the heteromonocyclic ring is unsubstituted or substituted with from 1 to 4 substituents independently selected from halogen, oxo, C_{1-4} alkyl, and -O-C_{1-4} alkyl;

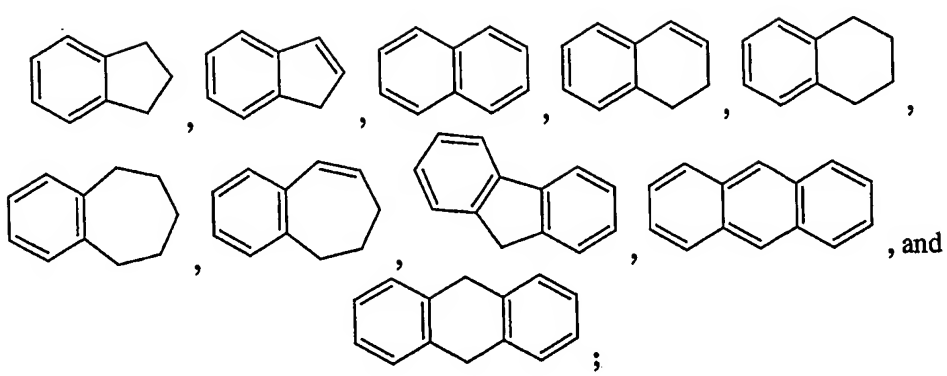
and all other variables are as originally defined or as defined in the first embodiment;

and with the proviso that when Z^1 is C-Q^3, Z^2 is C-Q^4, Z^3 is CH, and X is C-Q^1, then Y is not C-Q^2;

or a pharmaceutically acceptable salt thereof.

A third embodiment of the invention is a compound of Formula (I), wherein

A is phenyl or a fused carbocyclic ring system selected from the group consisting of



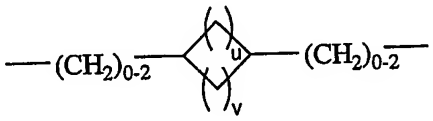
L is

(i) a single bond;

(ii) $-(CH_2)_{1-5}-$, which is optionally substituted with 1 or 2 substituents independently selected from the group consisting of halogen, -OH, $-C_{1-6}$ alkyl, $-O-C_{1-6}$ alkyl, $-CO_2R^a$, $-CO_2(CH_2)_{1-2}R^k$, $-C_{1-6}$ alkyl-OR^a, $-R^k$, $-(CH_2)_{1-2}R^k$, $-CH(OR^a)-R^k$, and $-CH(N(R^a)_2)-R^k$;

(iii) $-(CH_2)_{0-2}-CH=CH-(CH_2)_{1-2}-$, which is optionally substituted with 1 or 2 substituents independently selected from the group consisting of halogen, -OH, $-C_{1-6}$ alkyl, and $-O-C_{1-6}$ alkyl;

(iv)



, wherein u and v are each integers having a value from 0 to 4, provided that the sum of u + v is 1, 2, 3 or 4; or

(v) a heteroatom-containing chain which is $-(CH_2)_{0-3}N(R^a)-(CH_2)_{1-3}-$, $-(CH_2)_{1-2}-OC(=O)-(CH_2)_{1-2}-$, or $-(CH_2)_{1-2}-C(=O)O-(CH_2)_{1-2}-$;

R^5 is

(1) -H,

(2) $-C_{1-4}$ alkyl, optionally substituted with from 1 to 3 substituents independently selected from halogen, $-O-C_{1-6}$ alkyl, $-O-C_{1-6}$ fluoroalkyl, $-N(R^a)_2$, and $-CO_2R^a$;

(3) phenyl optionally substituted with from 1 to 5 substituents independently selected from halogen, C_{1-6} alkyl, C_{1-6} fluoroalkyl, -O-C_{1-6} alkyl, -O-C_{1-6} fluoroalkyl, -S-C_{1-6} alkyl, -CN, and -OH, or

(4) -C_{1-4} alkyl substituted with R^k;

each R^a is independently -H or -C_{1-6} alkyl;

each R^c is independently

(1) -H,

(2) -C_{1-4} alkyl,

(3) -C_{1-4} alkyl substituted with -$N(R^a)_2$, or

(4) -C_{1-4} alkyl-phenyl, wherein the phenyl is optionally substituted with 1 to 5 substituents independently selected from halogen, C_{1-6} alkyl, C_{1-6} fluoroalkyl, -O-C_{1-6} alkyl, -O-C_{1-6} fluoroalkyl, -S-C_{1-6} alkyl, -CN, and -OH;

each R^k is independently:

(1) aryl selected from phenyl and naphthyl, wherein aryl is unsubstituted or substituted with from 1 to 5 substituents independently selected from:

(a) halogen,

(b) C_{1-6} alkyl,

(c) C_{1-6} fluoroalkyl,

(d) -O-C_{1-6} alkyl,

(e) -O-C_{1-6} fluoroalkyl,

(f) phenyl,

(g) -S-C_{1-6} alkyl,

(h) -CN,

(i) -OH,

(j) phenyloxy, unsubstituted or substituted with from 1 to 3 substituents independently selected from:

(i) halogen,

(ii) C_{1-6} alkyl,

(iii) C_{1-6} fluoroalkyl, and

(iv) -OH,

(k) $-N(R^a)_2$,

(l) $-C_{1-6}$ alkyl-$N(R^a)_2$,

(m) $-R^t$,

(p) $-(CH_2)_{0-3}C(=O)N(R^a)_2$, and

(q) $-(CH_2)_{0-3}C(=O)R^a$;

(2) $-C_{3-7}$ cycloalkyl, unsubstituted or substituted with from 1 to 3 substituents independently selected from:

(a) halogen,

(b) C_{1-6} alkyl,

(c) -O-C_{1-6} alkyl,

(d) C_{1-6} fluoroalkyl,

(e) -O-C_{1-6} fluoroalkyl,

(f) -CN,

(h) phenyl, and

(j) -OH;

(3) $-C_{3-7}$ cycloalkyl fused with a phenyl ring, unsubstituted or substituted with from 1 to 5 substituents independently selected from:

(a) halogen,

(b) C_{1-6} alkyl,

(c) -O-C_{1-6} alkyl,

(d) C_{1-6} fluoroalkyl,

(e) -O-C_{1-6} fluoroalkyl,

(f) -CN, and

(g) -OH;

(4) a 5- or 6- membered heteroaromatic ring containing from 1 to 4 heteroatoms independently selected from oxygen, nitrogen and sulfur, wherein the heteroaromatic ring is unsubstituted or substituted on nitrogen or carbon with from 1 to 5 substituents independently selected from:

(a) halogen,

(b) C_{1-6} alkyl,

(c) C_{1-6} fluoroalkyl,

(d) -O-C_{1-6} alkyl,

(e) -O-C_{1-6} fluoroalkyl,

(f) phenyl,
(g) -S-C_{1-6} alkyl,
(h) -CN,
(i) -OH,
(j) phenyloxy, unsubstituted or substituted with from 1 to 3 substituents independently selected from:
(i) halogen,
(ii) C_{1-6} alkyl,
(iii) C_{1-6} fluoroalkyl, and
(iv) -OH,
(k) -$N(R^a)_2$,
(l) -C_{1-6} alkyl-$N(R^a)_2$,
(m) -R^t,
(n) oxo,
(o) -$(CH_2)_{0-3}C(=O)N(R^a)_2$, and
(p) -$(CH_2)_{0-3}C(=O)R^a$;

(5) a 5- or 6- membered saturated heterocyclic ring containing 1 or 2 heteroatoms independently selected from oxygen, nitrogen and sulfur, wherein the heterocyclic ring is unsubstituted or substituted with from 1 to 4 substituents independently selected from:
(a) halogen,
(b) C_{1-6} alkyl,
(c) -O-C_{1-6} alkyl,
(d) C_{1-6} fluoroalkyl,
(e) -O-C_{1-6} fluoroalkyl,
(f) -CN,
(g) oxo,
(h) phenyl
(i) benzyl,
(j) phenylethyl,
(k) -OH,
(l) -$(CH_2)_{0-3}C(=O)N(R^a)_2$,
(m) -$(CH_2)_{0-3}C(=O)R^a$,
(n) -$N(R^a)$-$C(=O)R^a$,

(o) $-N(R^a)-C(=O)OR^a$,
(p) $-(CH_2)_{1-3}N(R^a)-C(=O)R^a$,
(q) $-N(R^a)_2$,
(r) $-(CH_2)_{1-3}N(R^a)_2$,
(s) $-(CH_2)_{0-3}C(=O)R^t$,
(t) $-R^t$,
(u) $-N(R^a)R^t$, and
(v) $-(CH_2)_{1-3}R^t$; or

(6) an 8- to 10- membered heterobicyclic ring containing from 1 to 4 heteroatoms independently selected from oxygen, nitrogen and sulfur, wherein the heterobicyclic ring is saturated or unsaturated and is unsubstituted or substituted with from 1 to 5 substituents independently selected from:

(a) halogen,
(b) C_{1-6} alkyl,
(c) $-O-C_{1-6}$ alkyl,
(d) C_{1-6} fluoroalkyl,
(e) $-O-C_{1-6}$ fluoroalkyl,
(f) -CN,
(g) =O, and
(h) -OH; and

R^t is naphthyl or a 5- or 6-membered heteromonocylic ring containing from 1 to 4 nitrogen atoms, wherein the heteromonocyclic ring is saturated or unsaturated, and wherein either the naphthyl or the heteromonocyclic ring is unsubstituted or substituted with 1 or 2 substituents independently selected from halogen, oxo, C_{1-4} alkyl, and $-O-C_{1-4}$ alkyl;

and all other variables are as originally defined or as defined in the first embodiment;

and with the proviso that when Z^1 is $C-Q^3$, Z^2 is $C-Q^4$, Z^3 is CH, and X is $C-Q^1$, then Y is not $C-Q^2$;

or a pharmaceutically acceptable salt thereof.

A fourth embodiment of the present invention is a compound of Formula (I), wherein each R^k is independently:

(1) aryl selected from phenyl and naphthyl, wherein aryl is unsubstituted or substituted with from 1 to 4 substituents independently selected from:

(a) halogen,
(b) C_{1-6} alkyl,
(c) C_{1-6} haloalkyl,
(d) -O-C_{1-6} alkyl,
(e) -O-C_{1-6} haloalkyl,
(f) phenyl,
(g) -S-C_{1-6} alkyl,
(h) -CN,
(i) -OH,
(j) phenyloxy, unsubstituted or substituted with from 1 to 3 substituents independently selected from:
  (i) halogen,
  (ii) C_{1-6} alkyl,
  (iii) C_{1-6} haloalkyl, and
  (iv) -OH,
(k) -$N(R^a)_2$,
(l) -C_{1-6} alkyl-$N(R^a)_2$,
(m) -R^t,
(p) -$(CH_2)_{0-3}C(=O)N(R^a)_2$, and
(q) -$(CH_2)_{0-3}C(=O)R^a$;

(2) -C_{3-6} cycloalkyl, unsubstituted or substituted with from 1 to 3 substituents independently selected from:

(a) halogen,
(b) C_{1-6} alkyl,
(c) -O-C_{1-6} alkyl,
(d) C_{1-6} haloalkyl,
(e) -O-C_{1-6} haloalkyl,
(f) -CN,
(h) phenyl, and
(j) -OH;

(3) -C_{3-6} cycloalkyl fused with a phenyl ring, unsubstituted or substituted with from 1 to 4 substituents independently selected from:

(a) halogen,
(b) C_{1-6} alkyl,
(c) -O-C_{1-6} alkyl,
(d) C_{1-6} haloalkyl,
(e) -O-C_{1-6} haloalkyl,
(f) -CN, and
(g) -OH;

(4) a 5- or 6- membered heteroaromatic ring selected from thienyl, pyridyl, pyridyl N-oxide, imidazolyl, pyrrolyl, pyrazolyl, thiazolyl, isothiazolyl, oxazolyl, isooxazolyl, pyrazinyl, pyrimidinyl, triazolyl, tetrazolyl, furanyl, and pyridazinyl, wherein the heteroaromatic ring is unsubstituted or substituted on nitrogen or carbon with from 1 to 4 substituents independently selected from:

(a) halogen,
(b) C_{1-6} alkyl,
(c) C_{1-6} haloalkyl,
(d) -O-C_{1-6} alkyl,
(e) -O-C_{1-6} haloalkyl,
(f) phenyl,
(g) -S-C_{1-6} alkyl,
(h) -CN,
(i) -OH,
(j) phenyloxy, unsubstituted or substituted with from 1 to 3 substituents independently selected from:
  (i) halogen,
  (ii) C_{1-6} alkyl,
  (iii) C_{1-6} haloalkyl, and
  (iv) -OH,
(k) -$N(R^a)_2$,
(l) -C_{1-6} alkyl-$N(R^a)_2$,
(m) -R^t,
(n) oxo,
(o) -$(CH_2)_{0-3}C(=O)N(R^a)_2$, and

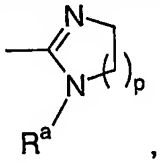
(p) $-(CH_2)_{0-3}C(=O)R^a$;

(5) a 5- or 6- or 7- membered saturated heterocyclic ring selected from piperidinyl, morpholinyl, thiomorpholinyl, thiazolidinyl, isothiazolidinyl, oxazolidinyl, isooxazolidinyl, pyrrolidinyl, imidazolidinyl, piperazinyl, tetrahydrofuranyl, pyrazolidinyl, hexahydropyrimidinyl, thiazinanyl, thiazepanyl, azepanyl, thiadiazepanyl, dithiazepanyl, diazepanyl, and thiadiazinanyl; and wherein the heterocyclic ring is unsubstituted or substituted with from 1 to 4 substituents independently selected from:

(a) halogen,
(b) C_{1-6} alkyl,
(c) $-O-C_{1-6}$ alkyl,
(d) C_{1-6} haloalkyl,
(e) $-O-C_{1-6}$ haloalkyl,
(f) -CN,
(g) oxo,
(h) phenyl
(i) benzyl,
(j) phenylethyl,
(k) -OH,
(l) $-(CH_2)_{0-3}C(=O)N(R^a)_2$,
(m) $-(CH_2)_{0-3}C(=O)R^a$,
(n) $-N(R^a)-C(=O)R^a$,
(o) $-N(R^a)-CO_2R^a$,
(p) $-(CH_2)_{1-3}N(R^a)-C(=O)R^a$,
(q) $-N(R^a)_2$,
(r) $-(CH_2)_{1-3}N(R^a)_2$,
(s) $-(CH_2)_{1-3}-OR^a$,
(t) $-(CH_2)_{0-3}CO_2R^a$,
(u) $-(CH_2)_{0-3}-O-(CH_2)_{1-3}-OR^a$,
(v) $-SO_2R^a$,
(w) $-SO_2N(R^a)_2$,
(x) $-(CH_2)_{0-3}C(=O)O(CH_2)_{1-2}CH=CH_2$,
(y) $-R^t$,
(z) $-(CH_2)_{0-3}C(=O)R^t$,

(aa) $-N(R^a)R^t$, and
(bb) $-(CH_2)_{1-3}R^t$;

(6) a mono-unsaturated heterocyclic ring which is:



wherein p is an integer from zero to 4 and wherein each ring carbon is optionally and independently substituted with $-C_{1-4}$ alkyl; or

(7) an 8- to 10- membered heterobicyclic ring selected from indolyl, benzotriazolyl, benzoimidazolyl, imidazo[4,5-b]pyridinyl, dihydroimidazo[4,5-b]pyridinyl, pyrazolo[4,3-c]pyridinyl, dihydropyrazolo[4,3-c]pyridinyl, tetrahydropyrazolo[4,3-c]pyridinyl, pyrrolo[1,2-a]pyrazinyl, dihydropyrrolo[1,2-a]pyrazinyl, tetrahydropyrrolo[1,2-a]pyrazinyl, octahydropyrrolo[1,2-a]pyrazinyl, isoindolyl, indazolyl, indolinyl, isoindolinyl, quinolinyl, isoquinolinyl, quinoxalinyl, quinazolinyl, cinnolinyl, chromanyl, isochromanyl, hexahydropyrazolo[4,3-c]pyridinyl, hexahydropurinyl, hexahydrooxazolo[3,4a]pyrazinyl, and 1,2,3,4-tetrahydro-1,8-naphthyridinyl; and wherein the bicyclic ring is unsubstituted or substituted with from 1 to 4 substituents independently selected from:

(a) halogen,
(b) C_{1-6} alkyl,
(c) $-O-C_{1-6}$ alkyl,
(d) C_{1-6} haloalkyl,
(e) $-O-C_{1-6}$ haloalkyl,
(f) -CN,
(g) =O, and
(h) -OH; and

R^t is naphthyl or a 5- or 6-membered heteromonocylic ring selected from pyrrolidinyl, pyrazolidinyl, imidazolinyl, piperidinyl, piperazinyl, pyrrolyl, pyridyl, imidazolyl, pyrazolyl, triazolyl, tetrazolyl, pyrazinyl, pyrimidinyl, and pyradizinyl; and wherein the naphthyl or the heteromonocyclic ring is unsubstituted or substituted with from 1 to 4 substituents independently selected from halogen, oxo, C_{1-4} alkyl, and $-O-C_{1-4}$ alkyl;

and all other variables are as originally defined or as defined in any one of the preceding embodiments;

and with the proviso that when Z^1 is C-Q^3, Z^2 is C-Q^4, Z^3 is CH, and X is C-Q^1, then Y is not C-Q^2;

or a pharmaceutically acceptable salt thereof.

In an aspect of the fourth embodiment, the compound of Formula (I) is as just defined above, except that in part (5) of the definition of R^k, the 5- or 6- or 7-membered saturated heterocyclic ring is selected from piperidinyl, morpholinyl, thiomorpholinyl, thiazolidinyl, isothiazolidinyl, oxazolidinyl, isooxazolidinyl, pyrrolidinyl, imidazolidinyl, piperazinyl, tetrahydrofuranyl, pyrazolidinyl, hexahydropyrimidinyl, thiazinanyl, thiazepanyl, and azepanyl.

A fifth embodiment of the present invention is a compound of Formula I, wherein each R^k is independently:

(1) aryl selected from phenyl and naphthyl, wherein aryl is unsubstituted or substituted with from 1 to 4 substituents independently selected from:
  (a) halogen,
  (b) C_{1-6} alkyl,
  (c) C_{1-6} fluoroalkyl,
  (d) -O-C_{1-6} alkyl,
  (e) -O-C_{1-6} fluoroalkyl,
  (f) phenyl,
  (g) -S-C_{1-6} alkyl,
  (h) -CN,
  (i) -OH,
  (j) phenyloxy, unsubstituted or substituted with from 1 to 3 substituents independently selected from:
    (i) halogen,
    (ii) C_{1-6} alkyl,
    (iii) C_{1-6} fluoroalkyl, and

(iv) -OH,

(k) $-N(R^a)_2$,

(l) $-C_{1-6}$ alkyl-$N(R^a)_2$,

(m) $-R^t$,

(p) $-(CH_2)_{0-3}C(=O)N(R^a)_2$, and

(q) $-(CH_2)_{0-3}C(=O)R^a$;

(2) $-C_{3-6}$ cycloalkyl, unsubstituted or substituted with from 1 to 3 substituents independently selected from:

(a) halogen,

(b) C_{1-6} alkyl,

(c) $-O-C_{1-6}$ alkyl,

(d) C_{1-6} fluoroalkyl,

(e) $-O-C_{1-6}$ fluoroalkyl,

(f) -CN,

(h) phenyl, and

(j) -OH;

(3) $-C_{3-6}$ cycloalkyl fused with a phenyl ring, unsubstituted or substituted with from 1 to 4 substituents independently selected from:

(a) halogen,

(b) C_{1-6} alkyl,

(c) $-O-C_{1-6}$ alkyl,

(d) C_{1-6} fluoroalkyl,

(e) $-O-C_{1-6}$ fluoroalkyl,

(f) -CN, and

(g) -OH;

(4) a 5- or 6- membered heteroaromatic ring selected from thienyl, pyridyl, imidazolyl, pyrrolyl, pyrazolyl, thiazolyl, isothiazolyl, oxazolyl, isooxazolyl, pyrazinyl, pyrimidinyl, triazolyl, tetrazolyl, furanyl, and pyridazinyl, wherein the heteroaromatic ring is unsubstituted or substituted on nitrogen or carbon with from 1 to 4 substituents independently selected from:

(a) halogen,

(b) C_{1-6} alkyl,

(c) C_{1-6} fluoroalkyl,

(d) $-O-C_{1-6}$ alkyl,

(e) -O-C_{1-6} fluoroalkyl,
(f) phenyl,
(g) -S-C_{1-6} alkyl,
(h) -CN,
(i) -OH,
(j) phenyloxy, unsubstituted or substituted with from 1 to 3 substituents independently selected from:
(i) halogen,
(ii) C_{1-6} alkyl,
(iii) C_{1-6} fluoroalkyl, and
(iv) -OH,
(k) -$N(R^a)_2$,
(l) -C_{1-6} alkyl-$N(R^a)_2$,
(m) -R^t,
(n) oxo,
(o) -$(CH_2)_{0-3}C(=O)N(R^a)_2$, and
(p) -$(CH_2)_{0-3}C(=O)R^a$;

(5) a 5- or 6- membered saturated heterocyclic ring selected from piperidinyl, morpholinyl, thiomorpholinyl, thiazolidinyl, isothiazolidinyl, oxazolidinyl, isooxazolidinyl, pyrrolidinyl, imidazolidinyl, piperazinyl, tetrahydrofuranyl, and pyrazolidinyl, wherein the heterocyclic ring is unsubstituted or substituted with from 1 to 3 substituents independently selected from:
(a) halogen,
(b) C_{1-6} alkyl,
(c) -O-C_{1-6} alkyl,
(d) C_{1-6} fluoroalkyl,
(e) -O-C_{1-6} fluoroalkyl,
(f) -CN,
(g) =O,
(h) phenyl
(i) benzyl,
(j) phenylethyl,
(k) -OH,
(l) -$(CH_2)_{0-3}C(=O)N(R^a)_2$,

(m) $-(CH_2)_{0-3}C(=O)R^a$,
(n) $N(R^a)-C(=O)R^a$,
(o) $N(R^a)-C(=O)OR^a$,
(p) $(CH_2)_{1-3}N(R^a)-C(=O)R^a$,
(q) $N(R^a)_2$,
(r) $(CH_2)_{1-3}N(R^a)_2$,
(s) $-(CH_2)_{0-3}C(=O)R^t$,
(t) $-R^t$,
(u) $-N(R^a)R^t$, and
(v) $-(CH_2)_{1-3}R^t$; or

(6) an 8- to 10- membered heterobicyclic ring selected from indolyl, benzotriazolyl, benzoimidazolyl, imidazo[4,5-b]pyridinyl, dihydroimidazo[4,5-b]pyridinyl, pyrazolo[4,3-c]pyridinyl, dihydropyrazolo[4,3-c]pyridinyl, tetrahydropyrazolo[4,3-c]pyridinyl, pyrrolo[1,2-a]pyrazinyl, dihydropyrrolo[1,2-a]pyrazinyl, tetrahydropyrrolo[1,2-a]pyrazinyl, octahydropyrrolo[1,2-a]pyrazinyl, isoindolyl, indazolyl, indolinyl, isoindolinyl, quinolinyl, isoquinolinyl, quinoxalinyl, quinazolinyl, cinnolinyl, chromanyl, and isochromanyl, wherein the bicyclic ring is unsubstituted or substituted with 1 or 2 substituents independently selected from:

(a) halogen,
(b) C_{1-6} alkyl,
(c) $-O-C_{1-6}$ alkyl,
(d) C_{1-6} fluoroalkyl,
(e) $-O-C_{1-6}$ fluoroalkyl,
(f) -CN,
(g) =O, and
(h) -OH; and

R^t is naphthyl or a 5- or 6-membered heteromonocylic ring selected from pyrrolidinyl, pyrazolidinyl, imidazolinyl, piperidinyl, piperazinyl, pyrrolyl, pyridyl, imidazolyl, pyrazolyl, triazolyl, tetrazolyl, pyrazinyl, pyrimidinyl, and pyradizinyl; and wherein the naphthyl or the heteromonocyclic ring is unsubstituted or substituted with 1 or 2 substituents independently selected from halogen, oxo, C_{1-4} alkyl, and $-O-C_{1-4}$ alkyl;

and all other variables are as originally defined or as defined in any one of the first, second, or third embodiments;

and with the proviso that when Z^1 is C-Q^3, Z^2 is C-Q^4, Z^3 is CH, and X is C-Q^1, then Y is not C-Q^2;

or a pharmaceutically acceptable salt thereof.

A sixth embodiment of the present invention is a compound of Formula (I), wherein

X is N;

Y is C-Q^2;

Z^1 is C-Q^3;

Z^2 is C-Q^4;

Z^3 is CH;

Q^2, Q^3, and Q^4 are as defined in (i) or (ii) as follows:

(i) Q^2 is

(1) -H,
(2) -C_{1-6} alkyl,
(3) -C_{1-6} fluoroalkyl,
(4) -O-C_{1-6} alkyl,
(5) -O-C_{1-6} fluoroalkyl,
(6) halo,
(7) -CN,
(8) -C_{1-6} alkyl-OR^a,
(9) -C_{0-6} alkyl-C(=O)R^a,

(10) -C_{0-6} alkyl-CO_2R^a,

(11) -C_{0-6} alkyl-SR^a,

(12) -$N(R^a)_2$,

(13) -C_{1-6} alkyl-$N(R^a)_2$,

(14) -C_{0-6} alkyl-$C(=O)N(R^a)_2$,

(15) -C_{0-6} alkyl-G-C_{1-6} alkyl-$C(=O)N(R^a)_2$, wherein G is O, S, $N(R^a)$, or $N(SO_2R^a)$,

(16) -$N(R^a)$-$C(R^a)$=O,

(17) -C_{1-6} alkyl-$N(R^a)$-$C(R^a)$=O,

(18) -C(=O)-$N(R^a)$-C_{1-6} alkyl-$[C(=O)]_{0-1}$-$N(R^a)_2$,

(19) -C(=O)-$N(R^a)$-C_{1-6} alkyl substituted with 1 or 2 -OR^a,

(20) -SO_2R^a,

(21) -$N(R^a)SO_2R^a$,

(22) -C_{2-6} alkenyl,

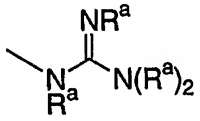
(23) -C_{2-6} alkenyl-C(=O)-$N(R^a)_2$,

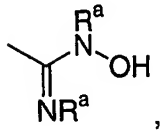
(24) -C_{2-5} alkynyl,

(25) -C_{2-5} alkynyl-$CH_2N(R^a)_2$,

(26) -C_{2-5} alkynyl-CH_2OR^a,

(27) -C_{2-5} alkynyl-$CH_2S(O)_n$-R^a,

(28)  ,

(29)  ,

(30) -$C(=NR^a)$-$N(R^a)_2$

(31) -$N(R^a)$-C_{1-6} alkyl-SR^a,

(32) -$N(R^a)$-C_{1-6} alkyl-OR^a,

(33) -$N(R^a)$-C_{1-6} alkyl-$N(R^a)_2$,

(34) -$N(R^a)$-C_{1-6} alkyl-$N(R^a)$-$C(R^a)$=O,

(35) -$N(R^a)$-C_{0-6} alkyl-$[C(=O)]_{1-2}N(R^a)_2$,

(36) -$N(R^a)$-C_{1-6} alkyl-CO_2R^a,

(37) -$N(R^a)C(=O)N(R^a)$-C_{1-6} alkyl-$C(=O)N(R^a)_2$,

(38) -$N(R^a)C(=O)$-C_{1-6} alkyl-$N(R^a)_2$,

(39) $-N(R^a)-SO_2-N(R^a)_2$,
(40) $-R^k$,
(41) $-C_{1-6}$ alkyl substituted with R^k,
(42) $-C_{1-6}$ fluoroalkyl substituted with R^k,
(43) $-C_{2-5}$ alkenyl-R^k,
(44) $-C_{2-5}$ alkynyl-R^k,
(45) $-O-R^k$,
(46) $-O-C_{1-4}$ alkyl-R^k,
(47) $-S(O)_n-R^k$,
(48) $-S(O)_n-C_{1-4}$ alkyl-R^k,
(49) $-O-C_{1-6}$ alkyl-OR^k,
(50) $-O-C_{1-6}$ alkyl-$O-C_{1-4}$ alkyl-R^k,
(51) $-O-C_{1-6}$ alkyl-$S(O)_nR^k$,
(52) $-N(R^c)-R^k$,
(53) $-N(R^c)-C_{1-6}$ alkyl substituted with one or two R^k groups,
(54) $-N(R^c)-C_{1-6}$ alkyl-OR^k,
(55) $-C(=O)-R^k$,
(56) $-C(=O)N(R^a)-R^k$,
(57) $-N(R^a)C(=O)-R^k$,
(58) $-C(=O)N(R^a)-C_{1-6}$ alkyl-R^k, or
(59) $-N(R^a)-C_{0-6}$ alkyl-$S(O)_nR^k$; and

each of Q^3 and Q^4 is independently:
(1) -H,
(2) $-C_{1-6}$ alkyl,
(3) $-C_{1-6}$ fluoroalkyl,
(4) $-O-C_{1-6}$ alkyl,
(5) $-O-C_{1-6}$ fluoroalkyl,
(6) halo,
(7) -CN,
(8) $-C_{1-6}$ alkyl-OR^a,
(9) $-C_{0-6}$ alkyl-$C(=O)R^a$,
(10) $-C_{0-6}$ alkyl-CO_2R^a,
(11) $-SR^a$,

(12) $-N(R^a)_2$,
(13) $-C_{1-6}$ alkyl $-N(R^a)_2$,
(14) $-C_{0-6}$ alkyl-$C(=O)N(R^a)_2$,
(15) $-SO_2R^a$,
(16) $-N(R^a)SO_2R^a$
(17) $-R^k$, or
(18) $-C_{1-6}$ alkyl substituted with R^k; or

(ii) alternatively, Q^2 and Q^3 together with the carbon atoms to which they are attached and the fused ring carbon atom therebetween form a 5- or 6-membered monocyclic carbocycle or a 5- or 6-membered monocyclic heterocycle, wherein the heterocycle contains 1 or 2 heteroatoms selected from nitrogen, oxygen and sulfur, and wherein either the carbocycle or heterocycle is optionally substituted with from 1 to 3 substituents independently selected from

(1) $-C_{1-6}$ alkyl,
(3) $-C_{1-6}$ fluoroalkyl,
(4) $-O-C_{1-6}$ alkyl,
(5) $-O-C_{1-6}$ fluoroalkyl,
(6) halo,
(7) -CN,
(8) $-C_{1-6}$ alkyl-OR^a,
(9) $-C_{1-6}$ alkyl-SR^a,
(10) $-C_{1-6}$ alkyl-$N(R^a)_2$,
(11) $-C_{1-6}$ alkyl-$C(=O)-N(R^a)_2$,
(12) $-C_{1-6}$ alkyl-CO_2R^a,
(13) oxo,
(14) $-R^k$, and
(15) $-C_{1-6}$ alkyl substituted with R^k; and

Q^4 is as defined in (i) above;

and all other variables are as originally defined or as defined in any one of the preceding embodiments;

or a pharmaceutically acceptable salt thereof.

In an aspect of the sixth embodiment, the compound of Formula (I) is as just defined above, except that part (i) of the definition of Q^2, Q^3, and Q^4 does not include (59) $-N(R^a)-C_{0-6}$ alkyl-$S(O)_nR^k$.

A seventh embodiment of the present invention is a compound of Formula I, wherein

X is N;

Y is C-Q^2;

Z^1 is C-Q^3;

Z^2 is C-Q^4;

Z^3 is CH;

Q^2 is

(1) -H,
(2) $-C_{1-6}$ alkyl,
(3) $-C_{1-6}$ fluoroalkyl,
(4) $-O-C_{1-6}$ alkyl,
(5) $-O-C_{1-6}$ fluoroalkyl,
(6) halo,
(7) -CN,
(8) $-C_{1-6}$ alkyl-OR^a,
(9) $-C_{0-6}$ alkyl-$C(=O)R^a$,
(10) $-C_{0-6}$ alkyl-CO_2R^a,
(11) $-C_{0-6}$ alkyl-SR^a,
(12) $-N(R^a)_2$,
(13) $-C_{1-6}$ alkyl $-N(R^a)_2$,
(14) $-C_{0-6}$ alkyl-$C(=O)N(R^a)_2$,

(15) -C_{1-6} alkyl-$N(R^a)$-$C(R^a)$=O,

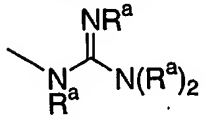
(16) -SO_2R^a,

(17) -$N(R^a)SO_2R^a$,

(18) -C_{2-5} alkynyl,

(19) -C_{2-5} alkynyl-$CH_2N(R^a)_2$,

(20) -C_{2-5} alkynyl-CH_2OR^a,

(21)  ,

(22) -$N(R^a)$-C_{1-6} alkyl-SR^a,

(23) -$N(R^a)$-C_{1-6} alkyl-OR^a,

(24) -$N(R^a)$-C_{1-6} alkyl-$N(R^a)_2$,

(25) -$N(R^a)$-C_{1-6} alkyl-$N(R^a)$-$C(R^a)$=O,

(26) -R^k,

(27) -C_{1-6} alkyl substituted with R^k,

(28) -C_{1-6} fluoroalkyl substituted with R^k,

(29) -C_{2-5} alkenyl-R^k,

(30) -C_{2-5} alkynyl-R^k,

(31) -O-R^k,

(32) -O-C_{1-4} alkyl-R^k,

(33) -$S(O)_n$-R^k,

(34) -$S(O)_n$-C_{1-4} alkyl-R^k,

(35) -O-C_{1-6} alkyl-OR^k,

(36) -O-C_{1-6} alkyl-O-C_{1-4} alkyl-R^k,

(37) -O-C_{1-6} alkyl-SR^k,

(38) -$N(R^c)$-R^k,

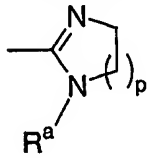
(39) -$N(R^c)$-C_{1-6} alkyl substituted with one or two R^k groups,

(40) -$N(R^c)$-C_{1-6} alkyl-OR^k,

(41) -C(=O)N-C_{1-6} alkyl-R^k,

(42) -C_{2-5} alkynyl-$CH_2S(O)_n$-R^a,

(43) -$C(=NR^a)$-$N(R^a)_2$, or

(44)  , wherein p is an integer from zero to 3;

each of Q^3 and Q^4 is independently:

(1) -H,
(2) -C_{1-6} alkyl,
(3) -C_{1-6} fluoroalkyl,
(4) -O-C_{1-6} alkyl,
(5) -O-C_{1-6} fluoroalkyl,
(6) halo,
(7) -CN,
(8) -C_{1-6} alkyl-OR^a,
(9) -C_{0-6} alkyl-$C(=O)R^a$,
(10) -C_{0-6} alkyl-CO_2R^a,
(11) -SR^a,
(12) -$N(R^a)_2$,
(13) -C_{1-6} alkyl -$N(R^a)_2$,
(14) -C_{0-6} alkyl-$C(=O)N(R^a)_2$,
(15) -SO_2R^a,
(16) -$N(R^a)SO_2R^a$
(17) -R^k, or
(18) -C_{1-6} alkyl substituted with R^k;

and all other variables are as defined in any one of the first, second, third, fourth, or fifth embodiments;

or a pharmaceutically acceptable salt thereof.

An eighth embodiment of the present invention is a compound of Formual (I), wherein

X is N;

Y is C-Q^2;

Z^1 is C-Q^3;

Z^2 is C-Q^4; and

Z^3 is CH;

and all other variables are as originally defined or as defined in any of the preceding embodiments;

or a pharmaceutically acceptable salt thereof.

In an aspect of the eighth embodiment, A is phenyl, and Q^3 and Q^4 are both -H.

A ninth embodiment of the present invention is a compound of Formula I, wherein:

Q^3 is:

(1) -H,
(2) -C_{1-6} alkyl,
(3) -C_{1-6} fluoroalkyl,
(4) -O-C_{1-6} alkyl,
(5) -O-C_{1-6} fluoroalkyl,
(6) halo,
(7) -CN,
(8) -C_{1-6} alkyl-OR^a,
(9) -C_{0-6} alkyl-$C(=O)R^a$,
(10) -C_{0-6} alkyl-CO_2R^a,
(11) -SR^a,
(12) -$N(R^a)_2$,
(13) -C_{1-6} alkyl -$N(R^a)_2$,
(14) -C_{0-6} alkyl-$C(=O)N(R^a)_2$,
(15) -SO_2R^a,
(16) -$N(R^a)SO_2R^a$
(17) -R^k, or

(18) -C_{1-6} alkyl substituted with R^k;

Q^4 is:

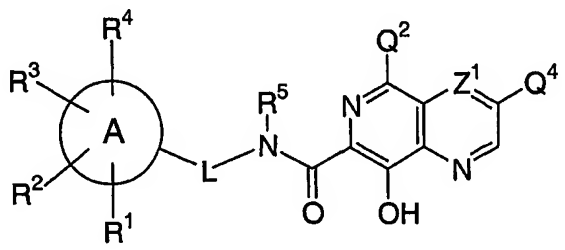
(1) -H,
(2) -C_{1-6} alkyl,
(3) -C_{1-6} fluoroalkyl,
(4) -O-C_{1-6} alkyl,
(5) -O-C_{1-6} fluoroalkyl,
(6) halo,
(7) -CN,
(8) -C_{1-6} alkyl-OR^a,
(9) -C_{0-6} alkyl-$C(=O)R^a$,
(10) -C_{0-6} alkyl-CO_2R^a,
(11) -SR^a,
(12) -$N(R^a)_2$,
(13) -C_{1-6} alkyl -$N(R^a)_2$,
(14) -C_{0-6} alkyl-$C(=O)N(R^a)_2$,
(15) -SO_2R^a, or
(16) -$N(R^a)SO_2R^a$;

and all other variables are as defined in the seventh embodiment;

or a pharmaceutically acceptable salt thereof.

In an aspect of the ninth embodiment, Q^3 and Q^4 are both -H.

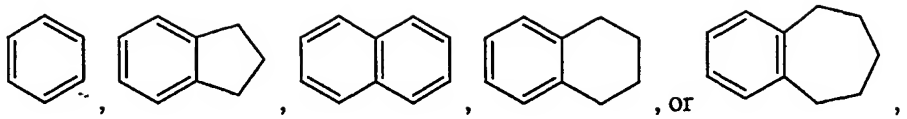
A tenth embodiment of the present invention is a compound of Formula (II):



(II),

wherein

A is



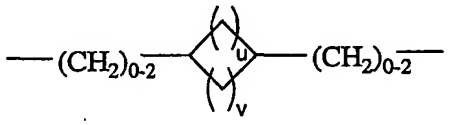
L is

(i) a single bond;

(ii) $-(CH_2)_{1-3}-$, which is optionally substituted with 1 or 2 substituents independently selected from the group consisting of halogen, -OH, $-C_{1-4}$ alkyl, $-O-C_{1-4}$ alkyl, $-CO_2CH_3$, $-CO_2CH_2$-phenyl, phenyl, benzyl, $-(CH_2)_{1-2}OH$, -CH(OH)-phenyl, and $-CH(NH_2)$-phenyl;

(iii) $-(CH_2)_{0-1}-CH=CH-(CH_2)-$, which is optionally substituted with 1 or 2 substituents independently selected from the group consisting of halogen, -OH, $-C_{1-4}$ alkyl, and $-O-C_{1-4}$ alkyl;

(iv)



, wherein u and v are each integers having a value of from 0 to 4, provided that the sum of u + v is 1, 2, 3 or 4; or

(v) a heteroatom-containing chain which is $-N(R^a)-(CH_2)_{1-2}-$, $-CH_2-OC(=O)-CH_2-$, or $-CH_2-C(=O)O-CH_2-$;

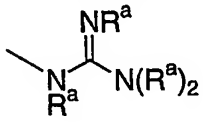
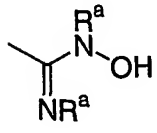
Z^1 is N or C-Q^3;

Q^2 and Q^3 are as defined in (i) or (ii) as follows:

(i) Q^2 is

(1) -H,

(2) $-C_{1-4}$ alkyl,

(3) -C_{1-4} fluoroalkyl,
(4) -O-C_{1-4} alkyl,
(5) -O-C_{1-4} fluoroalkyl,
(6) halo,
(7) -CN,
(8) -C_{1-4} alkyl-OR^a,
(9) -$(CH_2)_{0-2}C(=O)R^a$,
(10) -$(CH_2)_{0-2}CO_2R^a$,
(11) -$(CH_2)_{0-2}SR^a$,
(12) -$N(R^a)_2$,
(13) -C_{1-4} alkyl -$N(R^a)_2$,
(14) -$(CH_2)_{0-2}C(=O)N(R^a)_2$,
(15) -G-C_{1-6} alkyl-$C(=O)N(R^a)_2$, wherein G is O, S, $N(R^a)$, or $N(SO_2R^a)$,
(16) -$N(R^a)$-$C(R^a)$=O,
(17) -$(CH_2)_{1-3}$-$N(R^a)$-$C(R^a)$=O,
(18) -C(=O)-$N(R^a)$-$(CH_2)_{1-3}$-$[C(=O)]_{0-1}$-$N(R^a)_2$,
(19) -C(=O)-$N(R^a)$-C_{1-4} alkyl substituted with 1 or 2 -OR^a,
(20) -SO_2R^a,
(21) -$N(R^a)SO_2R^a$,
(22) -C_{2-4} alkenyl,
(23) -C_{2-4} alkenyl-$C(=O)$-$N(R^a)_2$,
(24) -C_{2-3} alkynyl,
(25) $—C\equiv C—CH_2N(R^a)_2$,
(26) $—C\equiv C—CH_2OR^a$,
(27) $—C\equiv C—CH_2SR^a$,
(28) $—C\equiv C—CH_2SO_2R^a$,
(29)  ,
(30)  ,
(31) -$N(R^a)$-C_{1-4} alkyl-SR^a,

(32) -N(R^a)-C_{1-4} alkyl-OR^a,
(33) -N(R^a)-C_{1-4} alkyl-N(R^a)2,
(34) -N(R^a)-C_{1-4} alkyl-N(R^a)-C(R^a)=O,
(35) -N(R^a)-C_{0-4} alkyl-[C(=O)]1-2N(R^a)2,
(36) -N(R^a)-C_{1-4} alkyl-CO_2R^a,
(37) -N(R^a)C(=O)N(R^a)-C_{1-4} alkyl-C(=O)N(R^a)2,
(38) -N(R^a)C(=O)-C_{1-4} alkyl-N(R^a)2,
(39) -N(R^a)-SO_2-N(R^a)2,
(40) -R^k,
(41) -C_{1-4} alkyl substituted with R^k,
(42) -C_{1-4} fluoroalkyl substituted with R^k,
(43) -C_{2-5} alkenyl-R^k,
(44) -C_{2-5} alkynyl-R^k,
(45) -O-R^k,
(46) -O-C_{1-4} alkyl-R^k,
(47) -S(O)n-R^k,
(48) -S(O)n-C_{1-4} alkyl-R^k,
(49) -O-C_{1-4} alkyl-OR^k,
(50) -O-C_{1-4} alkyl-O-C_{1-4} alkyl-R^k,
(51) -O-C_{1-4} alkyl-S(O)nR^k,
(52) -N(R^c)-R^k,
(53) -N(R^c)-C_{1-4} alkyl substituted with one or two R^k groups,
(54) -N(R^c)-C_{1-4} alkyl-OR^k,
(55) -C(=O)-R^k,
(56) -C(=O)N(R^a)-R^k,
(57) -N(R^a)C(=O)-R^k,
(58) -C(=O)N(R^a)-C_{1-4} alkyl-R^k, or
(59) -N(R^a)-C_{0-4} alkyl-S(O)nR^k;

Q^3 is
(1) -H,
(2) -C_{1-4} alkyl,
(3) -C_{1-4} fluoroalkyl,
(4) -O-C_{1-4} alkyl,

(5) -O-C_{1-4} fluoroalkyl,
(6) halo selected from -F, -Cl, and -Br,
(7) -CN,
(8) -C_{1-4} alkyl-OR^a, or
(9) -C_{1-4} alkyl substituted with R^k; or

(ii) alternatively, Q^2 and Q^3 together with the carbon atoms to which they are attached and the fused ring carbon atom attached therebetween form a 5- or 6-membered monocyclic heterocycle, wherein the heterocycle contains 1 or 2 heteroatoms selected from nitrogen, oxygen and sulfur, and wherein the heterocycle is optionally substituted with from 1 to 3 substituents independently selected from
(1) -C_{1-4} alkyl,
(3) -C_{1-4} fluoroalkyl,
(4) -O-C_{1-4} alkyl,
(5) -O-C_{1-4} fluoroalkyl,
(6) halo,
(7) -CN,
(8) -C_{1-4} alkyl-OR^a,
(9) -C_{1-4} alkyl-$S(O)_nR^a$,
(10) -C_{1-4} alkyl-$N(R^a)_2$,
(11) -C_{1-4} alkyl-$C(=O)$-$N(R^a)_2$,
(12) -C_{1-4} alkyl-CO_2R^a,
(13) oxo,
(14) -R^k, and
(15) -C_{1-4} alkyl substituted with R^k;

Q^4 is:
(1) -H,
(2) -C_{1-4} alkyl,
(3) -C_{1-4} fluoroalkyl,
(4) -O-C_{1-4} alkyl,
(5) -O-C_{1-4} fluoroalkyl,
(6) halo selected from -F, -Cl, and -Br,
(7) -CN,

(8) -C_{1-6} alkyl-OR^a,
(9) -$N(R^a)_2$, or
(10) -C_{1-6} alkyl -$N(R^a)_2$;

each of R^1 and R^2 is independently:
(1) -H,
(2) -C_{1-4} alkyl,
(3) -C_{1-4} fluoroalkyl,
(4) -O-C_{1-4} alkyl,
(5) -O-C_{1-4} fluoroalkyl,
(6) -OH,
(7) halo,
(8) -CN,
(9) -C_{1-4} alkyl-OR^a,
(10) -$(CH_2)_{0-2}C(=O)R^a$,
(11) -$(CH_2)_{0-2}CO_2R^a$,
(12) -$(CH_2)_{0-2}SR^a$,
(13) -$N(R^a)_2$,
(14) -C_{1-4} alkyl $N(R^a)_2$,
(15) -$(CH_2)_{0-2}C(=O)N(R^a)_2$,
(16) -C_{1-4} alkyl-$N(R^a)$-$C(R^a)$=O,
(17) -SO_2R^a,
(18) -$N(R^a)SO_2R^a$,
(19) -O-C_{1-4} alkyl-OR^a,
(20) -O-C_{1-4} alkyl-SR^a,
(21) -O-C_{1-4} alkyl-NH-CO_2R^a,
(22) -O-C_{2-4} alkyl-$N(R^a)_2$,
(23) -$N(R^a)$-C_{1-4} alkyl-SR^a,
(24) -$N(R^a)$-C_{1-4} alkyl-OR^a,
(25) -$N(R^a)$-C_{1-4} alkyl-$N(R^a)_2$,
(26) -$N(R^a)$-C_{1-4} alkyl-$N(R^a)$-$C(R^a)$=O,
(27) -R^k,
(28) -C_{1-4} alkyl substituted with 1 or 2 R^k groups,
(29) -C_{1-4} fluoroalkyl substituted with 1 or 2 R^k groups,

(30) -O-R^k,
(31) -O-C_{1-4} alkyl-R^k,
(32) -$S(O)_n$-R^k,
(33) -$S(O)_n$-C_{1-4} alkyl-R^k,
(34) -O-C_{1-4} alkyl-OR^k,
(35) -O-C_{1-4} alkyl-O-C_{1-4} alkyl-R^k,
(36) -O-C_{1-4} alkyl-$S(O)_nR^k$, or
(37) -C_{0-4} alkyl-$N(R^b)(R^k)$;

each of R^3 and R^4 is independently
(1) -H,
(2) halo,
(3) -CN,
(4) -OH,
(5) C_{1-4} alkyl,
(6) C_{1-4} fluoroalkyl,
(7) -O-C_{1-4} alkyl,
(8) -O-C_{1-4} fluoroalkyl,
(9) -C_{1-4} alkyl-OR^a,
(10) -O-C_{1-4} alkyl-OR^a,
(11) -O-C_{1-4} alkyl-SR^a,
(12) -O-C_{1-4} alkyl-NH-CO_2R^a, or
(13) -O-C_{2-4} alkyl-$N(R^a)_2$;

R^5 is
(1) -H,
(2) -C_{1-4} alkyl, optionally substituted with 1 or 2 substituents independently selected from halogen, -O-C_{1-4} alkyl, -O-C_{1-4} fluoroalkyl, -$N(R^a)_2$, and -CO_2R^a;
(3) phenyl optionally substituted with from 1 to 3 substituents independently selected from halogen, C_{1-4} alkyl, C_{1-4} fluoroalkyl, -O-C_{1-4} alkyl, -O-C_{1-4} fluoroalkyl, -S-C_{1-4} alkyl, -CN, and -OH, or
(4) -C_{1-4} alkyl substituted with phenyl;

each R^a is independently -H or -C_{1-4} alkyl;

each R^b is independently:

(1) -H,
(2) -C_{1-4} alkyl,
(3) -C_{1-4} fluoroalkyl,
(4) -R^k,
(5) -C_{1-4} alkyl-R^k,
(6) -$S(O)_n$-R^k, or
(7) -C(=O)-R^k;

each R^c is independently

(1) -H,
(2) -C_{1-4} alkyl,
(3) -C_{1-4} alkyl substituted with -$N(R^a)_2$, or
(4) -C_{1-4} alkyl-phenyl, wherein the phenyl is optionally substituted with 1 to 3 substituents independently selected from halogen, C_{1-4} alkyl, C_{1-4} fluoroalkyl, -O-C_{1-4} alkyl, -O-C_{1-4} fluoroalkyl, -S-C_{1-4} alkyl, -CN, and -OH;

each R^k is independently:

(1) aryl selected from phenyl and naphthyl, wherein aryl is unsubstituted or substituted with from 1 to 5 substituents independently selected from:

(a) halogen,
(b) C_{1-6} alkyl,
(c) C_{1-6} fluoroalkyl,
(d) -O-C_{1-6} alkyl,
(e) -O-C_{1-6} fluoroalkyl,
(f) phenyl,
(g) -S-C_{1-6} alkyl,
(h) -CN,
(i) -OH,

(j) phenyloxy, unsubstituted or substituted with from 1 to 3 substituents independently selected from:
(i) halogen,
(ii) C_{1-6} alkyl,
(iii) C_{1-6} fluoroalkyl, and
(iv) -OH,
(k) $-N(R^a)_2$,
(l) $-C_{1-6}$ alkyl-$N(R^a)_2$,
(m) $-R^t$,
(p) $-(CH_2)_{0-3}C(=O)N(R^a)_2$, and
(q) $-(CH_2)_{0-3}C(=O)R^a$;

(2) $-C_{3-7}$ cycloalkyl, unsubstituted or substituted with from 1 to 3 substituents independently selected from:
(a) halogen,
(b) C_{1-6} alkyl,
(c) $-O-C_{1-6}$ alkyl,
(d) C_{1-6} fluoroalkyl,
(e) $-O-C_{1-6}$ fluoroalkyl,
(f) -CN,
(h) phenyl, and
(j) -OH;

(3) $-C_{3-7}$ cycloalkyl fused with a phenyl ring, unsubstituted or substituted with from 1 to 5 substituents independently selected from:
(a) halogen,
(b) C_{1-6} alkyl,
(c) $-O-C_{1-6}$ alkyl,
(d) C_{1-6} fluoroalkyl,
(e) $-O-C_{1-6}$ fluoroalkyl,
(f) -CN, and
(g) -OH;

(4) a 5- or 6- membered heteroaromatic ring containing from 1 to 4 heteroatoms independently selected from oxygen, nitrogen and sulfur, wherein the heteroaromatic ring is unsubstituted or substituted on nitrogen or carbon with from 1 to 5 substituents independently selected from:

(a) halogen,
(b) C_{1-6} alkyl,
(c) C_{1-6} fluoroalkyl,
(d) -O-C_{1-6} alkyl,
(e) -O-C_{1-6} fluoroalkyl,
(f) phenyl,
(g) -S-C_{1-6} alkyl,
(h) -CN,
(i) -OH,
(j) phenyloxy, unsubstituted or substituted with from 1 to 3 substituents independently selected from:
(i) halogen,
(ii) C_{1-6} alkyl,
(iii) C_{1-6} fluoroalkyl, and
(iv) -OH,
(k) -$N(R^a)_2$,
(l) -C_{1-6} alkyl-$N(R^a)_2$,
(m) -R^t,
(n) oxo,
(o) -$(CH_2)_{0-3}C(=O)N(R^a)_2$, and
(p) -$(CH_2)_{0-3}C(=O)R^a$;

(5) a 5- or 6- or 7- membered saturated heterocyclic ring containing from 1 to 3 heteroatoms independently selected from oxygen, nitrogen and sulfur, wherein the heterocyclic ring is unsubstituted or substituted with from 1 to 4 substituents independently selected from:

(a) halogen,
(b) C_{1-6} alkyl,
(c) -O-C_{1-6} alkyl,
(d) C_{1-6} fluoroalkyl,
(e) -O-C_{1-6} fluoroalkyl,
(f) -CN,
(g) oxo,
(h) phenyl
(i) benzyl,

(j) phenylethyl,
(k) -OH,
(l) $-(CH_2)_{0-3}C(=O)N(R^a)_2$,
(m) $-(CH_2)_{0-3}C(=O)R^a$,
(n) $-N(R^a)-C(=O)R^a$,
(o) $-N(R^a)-CO_2R^a$,
(p) $-(CH_2)_{1-3}N(R^a)-C(=O)R^a$,
(q) $-N(R^a)_2$,
(r) $-(CH_2)_{1-3}N(R^a)_2$,
(s) $-(CH_2)_{1-3}-OR^a$,
(t) $-(CH_2)_{0-3}CO_2R^a$,
(u) $-(CH_2)_{0-3}-O-(CH_2)_{1-3}-OR^a$,
(v) $-SO_2R^a$,
(w) $-SO_2N(R^a)_2$,
(x) $-(CH_2)_{0-3}C(=O)O(CH_2)_{1-2}CH=CH_2$,
(y) $-R^t$,
(z) $-(CH_2)_{0-3}C(=O)R^t$,
(aa) $-N(R^a)R^t$, and
(bb) $-(CH_2)_{1-3}R^t$; or

(6) an 8- to 10- membered heterobicyclic ring containing from 1 to 4 heteroatoms independently selected from oxygen, nitrogen and sulfur, wherein the heterobicyclic ring is saturated or unsaturated, and is unsubstituted or substituted with from 1 to 5 substituents independently selected from:

(a) halogen,
(b) C_{1-6} alkyl,
(c) $-O-C_{1-6}$ alkyl,
(d) C_{1-6} fluoroalkyl,
(e) $-O-C_{1-6}$ fluoroalkyl,
(f) -CN,
(g) =O, and
(h) -OH;

R^t is naphthyl or a 5- or 6-membered heteromonocylic ring containing from 1 to 4 nitrogen atoms, wherein the heteromonocyclic ring is saturated or unsaturated, and

wherein the naphthyl or the heteromonocyclic ring is unsubstituted or substituted with from 1 to 4 substituents independently selected from halogen, oxo, C_{1-4} alkyl, and -O-C_{1-4} alkyl; and

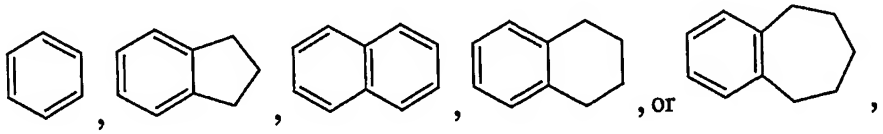
n is an integer equal to 0, 1 or 2;

or a pharmaceutically acceptable salt thereof.

In an aspect of the tenth embodiment, the compound of Formula (II) is as just defined above, except that part (i) of the definition of Q^2 does not include (59) -$N(R^a)$-C_{0-4} alkyl-$S(O)_nR^k$.

An eleventh embodiment of the present invention is a compound of Formula (II), wherein

A is



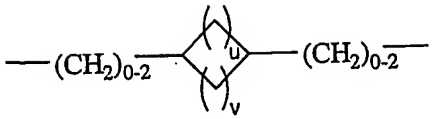
L is

(i) a single bond;

(ii) -$(CH_2)_{1-3}$-, which is optionally substituted with 1 or 2 substituents independently selected from the group consisting of -OH, -C_{1-4} alkyl, -O-C_{1-4} alkyl, -CO_2CH_3, -CO_2CH_2-phenyl, phenyl, benzyl, -$(CH_2)_{1-2}$OH, -CH(OH)-phenyl, and -$CH(NH_2)$-phenyl;

(iii) -$(CH_2)_{0-1}$-CH=CH-(CH_2)-, which is optionally substituted with 1 or 2 substituents independently selected from the group consisting of halogen, -OH, -C_{1-4} alkyl, and -O-C_{1-4} alkyl;

(iv)



, wherein u and v are each integers having a value of from 0 to 4, provided that the sum of u + v is 1, 2, 3 or 4; or

(v) a heteroatom-containing chain which is $-N(R^a)-(CH_2)_{1-2}-$, $-CH_2-OC(=O)-CH_2-$, or $-CH_2-C(=O)O-CH_2-$;

Z^1 is N or C-Q^3;

Q^2 is

(1) -H,
(2) -C_{1-4} alkyl,
(3) -C_{1-4} fluoroalkyl,
(4) -O-C_{1-4} alkyl,
(5) -O-C_{1-4} fluoroalkyl,
(6) halo,
(7) -CN,
(8) -C_{1-4} alkyl-OR^a,
(9) -$(CH_2)_{0-2}C(=O)R^a$,
(10) -$(CH_2)_{0-2}CO_2R^a$,
(11) -$(CH_2)_{0-2}SR^a$,
(12) -$N(R^a)_2$,
(13) -C_{1-4} alkyl -$N(R^a)_2$,
(14) -$(CH_2)_{0-2}C(=O)N(R^a)_2$,
(15) -SO_2R^a,
(16) -$N(R^a)SO_2R^a$,
(17) -C_{2-3} alkynyl,
(18) $-C\equiv C-CH_2N(R^a)_2$,
(19) $-C\equiv C-CH_2OR^a$,
(20) -$N(R^a)$-C_{1-4} alkyl-SR^a,
(21) -$N(R^a)$-C_{1-4} alkyl-OR^a,
(22) -$N(R^a)$-C_{1-4} alkyl-$N(R^a)_2$,
(23) -$N(R^a)$-C_{1-4} alkyl-$N(R^a)$-$C(R^a)$=O,

(24) -R^k,
(25) -C_{1-4} alkyl substituted with R^k,
(26) -C_{1-4} fluoroalkyl substituted with R^k,
(27) -C_{2-5} alkenyl-R^k,
(28) -C_{2-5} alkynyl-R^k,
(29) -O-R^k,
(30) -O-C_{1-4} alkyl-R^k,
(31) -$S(O)_n$-R^k,
(32) -$N(R^c)$-R^k,
(33) -$N(R^c)$-C_{1-4} alkyl substituted with one or two R^k groups,
(34) -$N(R^c)$-C_{1-4} alkyl-OR^k,
(35) -C(=O)N-C_{1-4} alkyl-R^k,
(36) $—C{\equiv}C-CH_2SR^a$, or
(37) $—C{\equiv}C-CH_2SO_2R^a$;

Q^3 is

(1) -H,
(2) -C_{1-4} alkyl,
(3) -C_{1-4} fluoroalkyl,
(4) -O-C_{1-4} alkyl,
(5) -O-C_{1-4} fluoroalkyl,
(6) halo selected from -F, -Cl, and -Br,
(7) -CN,
(8) -C_{1-4} alkyl-OR^a, or
(9) -C_{1-4} alkyl substituted with R^k;

Q^4 is:

(1) -H,
(2) -C_{1-4} alkyl,
(3) -C_{1-4} fluoroalkyl,
(4) -O-C_{1-4} alkyl,
(5) -O-C_{1-4} fluoroalkyl,
(6) halo selected from -F, -Cl, and -Br,
(7) -CN,

(8) -C_{1-6} alkyl-OR^a,
(9) -$N(R^a)_2$, or
(10) -C_{1-6} alkyl -$N(R^a)_2$;

each of R^1 and R^2 is independently:
(1) -H,
(2) -C_{1-4} alkyl,
(3) -C_{1-4} fluoroalkyl,
(4) -O-C_{1-4} alkyl,
(5) -O-C_{1-4} fluoroalkyl,
(6) -OH,
(7) halo,
(8) -CN,
(9) -C_{1-4} alkyl-OR^a,
(10) -$(CH_2)_{0-2}C(=O)R^a$,
(11) -$(CH_2)_{0-2}CO_2R^a$,
(12) -$(CH_2)_{0-2}SR^a$,
(13) -$N(R^a)_2$,
(14) -C_{1-4} alkyl $N(R^a)_2$,
(15) -$(CH_2)_{0-2}C(=O)N(R^a)_2$,
(16) -C_{1-4} alkyl-$N(R^a)$-$C(R^a)$=O,
(17) -SO_2R^a,
(18) -$N(R^a)SO_2R^a$,
(19) -O-C_{1-4} alkyl-OR^a,
(20) -O-C_{1-4} alkyl-SR^a,
(21) -O-C_{1-4} alkyl-NH-CO_2R^a,
(22) -O-C_{2-4} alkyl-$N(R^a)_2$,
(23) -$N(R^a)$-C_{1-4} alkyl-SR^a,
(24) -$N(R^a)$-C_{1-4} alkyl-OR^a,
(25) -$N(R^a)$-C_{1-4} alkyl-$N(R^a)_2$,
(26) -$N(R^a)$-C_{1-4} alkyl-$N(R^a)$-$C(R^a)$=O,
(27) -R^k,
(28) -C_{1-4} alkyl substituted with 1 or 2 R^k groups,
(29) -C_{1-4} fluoroalkyl substituted with 1 or 2 R^k groups,

(30) -O-R^k,
(31) -O-C_{1-4} alkyl-R^k,
(32) -S(O)$_n$-R^k,
(33) -S(O)$_n$-C_{1-4} alkyl-R^k,
(34) -O-C_{1-4} alkyl-OR^k,
(35) -O-C_{1-4} alkyl-O-C_{1-4} alkyl-R^k,
(36) -O-C_{1-4} alkyl-SR^k, or
(37) -C_{0-4} alkyl-N(R^b)(R^k);

each of R^3 and R^4 is independently
(1) -H,
(2) halo,
(3) -CN,
(4) -OH,
(5) C_{1-4} alkyl,
(6) C_{1-4} fluoroalkyl,
(7) -O-C_{1-4} alkyl,
(8) -O-C_{1-4} fluoroalkyl,
(9) -C_{1-4} alkyl-OR^a,
(10) -O-C_{1-4} alkyl-OR^a,
(11) -O-C_{1-4} alkyl-SR^a,
(12) -O-C_{1-4} alkyl-NH-CO_2R^a, or
(13) -O-C_{2-4} alkyl-N(R^a)2;

R^5 is
(1) -H,
(2) -C_{1-4} alkyl, optionally substituted with 1 or 2 substituents independently selected from halogen, -O-C_{1-4} alkyl, -O-C_{1-4} fluoroalkyl, -N(R^a)2, and -CO_2R^a;
(3) phenyl optionally substituted with from 1 to 3 substituents independently selected from halogen, C_{1-4} alkyl, C_{1-4} fluoroalkyl, -O-C_{1-4} alkyl, -O-C_{1-4} fluoroalkyl, -S-C_{1-4} alkyl, -CN, and -OH, or
(4) -C_{1-4} alkyl substituted with phenyl;

each R^a is independently -H or -C_{1-4} alkyl;

each R^b is independently:

(1) -H,
(2) -C_{1-4} alkyl,
(3) -C_{1-4} fluoroalkyl,
(4) -R^k,
(5) -C_{1-4} alkyl-R^k,
(6) -$S(O)_n$-R^k, or
(7) -C(=O)-R^k;

each R^c is independently

(1) -H,
(2) -C_{1-4} alkyl,
(3) -C_{1-4} alkyl substituted with -$N(R^a)_2$, or
(4) -C_{1-4} alkyl-phenyl, wherein the phenyl is optionally substituted with 1 to 3 substituents independently selected from halogen, C_{1-4} alkyl, C_{1-4} fluoroalkyl, -O-C_{1-4} alkyl, -O-C_{1-4} fluoroalkyl, -S-C_{1-4} alkyl, -CN, and -OH;

each R^k is independently:

(1) aryl selected from phenyl and naphthyl, wherein aryl is unsubstituted or substituted with from 1 to 5 substituents independently selected from:

(a) halogen,
(b) C_{1-6} alkyl,
(c) C_{1-6} fluoroalkyl,
(d) -O-C_{1-6} alkyl,
(e) -O-C_{1-6} fluoroalkyl,
(f) phenyl,
(g) -S-C_{1-6} alkyl,
(h) -CN,
(i) -OH,

(j) phenyloxy, unsubstituted or substituted with from 1 to 3 substituents independently selected from:
(i) halogen,
(ii) C_{1-6} alkyl,
(iii) C_{1-6} fluoroalkyl, and
(iv) -OH,
(k) $-N(R^a)_2$,
(l) $-C_{1-6}$ alkyl-$N(R^a)_2$,
(m) $-R^t$,
(p) $-(CH_2)_{0-3}C(=O)N(R^a)_2$, and
(q) $-(CH_2)_{0-3}C(=O)R^a$;

(2) $-C_{3-7}$ cycloalkyl, unsubstituted or substituted with from 1 to 3 substituents independently selected from:
(a) halogen,
(b) C_{1-6} alkyl,
(c) $-O-C_{1-6}$ alkyl,
(d) C_{1-6} fluoroalkyl,
(e) $-O-C_{1-6}$ fluoroalkyl,
(f) -CN,
(h) phenyl, and
(j) -OH;

(3) $-C_{3-7}$ cycloalkyl fused with a phenyl ring, unsubstituted or substituted with from 1 to 5 substituents independently selected from:
(a) halogen,
(b) C_{1-6} alkyl,
(c) $-O-C_{1-6}$ alkyl,
(d) C_{1-6} fluoroalkyl,
(e) $-O-C_{1-6}$ fluoroalkyl,
(f) -CN, and
(g) -OH;

(4) a 5- or 6- membered heteroaromatic ring containing from 1 to 4 heteroatoms independently selected from oxygen, nitrogen and sulfur, wherein the heteroaromatic ring is unsubstituted or substituted on nitrogen or carbon with from 1 to 5 substituents independently selected from:

(a) halogen,
(b) C_{1-6} alkyl,
(c) C_{1-6} fluoroalkyl,
(d) -O-C_{1-6} alkyl,
(e) -O-C_{1-6} fluoroalkyl,
(f) phenyl,
(g) -S-C_{1-6} alkyl,
(h) -CN,
(i) -OH,
(j) phenyloxy, unsubstituted or substituted with from 1 to 3 substituents independently selected from:
(i) halogen,
(ii) C_{1-6} alkyl,
(iii) C_{1-6} fluoroalkyl, and
(iv) -OH,
(k) -$N(R^a)_2$,
(l) -C_{1-6} alkyl-$N(R^a)_2$,
(m) -R^t,
(n) oxo,
(o) -$(CH_2)_{0-3}C(=O)N(R^a)_2$, and
(p) -$(CH_2)_{0-3}C(=O)R^a$;

(5) a 5- or 6- membered saturated heterocyclic ring containing 1 or 2 heteroatoms independently selected from oxygen, nitrogen and sulfur, wherein the heterocyclic ring is unsubstituted or substituted with from 1 to 4 substituents independently selected from:
(a) halogen,
(b) C_{1-6} alkyl,
(c) -O-C_{1-6} alkyl,
(d) C_{1-6} fluoroalkyl,
(e) -O-C_{1-6} fluoroalkyl,
(f) -CN,
(g) oxo,
(h) phenyl,
(i) benzyl,

(j) phenylethyl,
(k) -OH,
(l) $-(CH_2)_{0-3}C(=O)N(R^a)_2$,
(m) $-(CH_2)_{0-3}C(=O)R^a$,
(n) $-N(R^a)-C(=O)R^a$,
(o) $-N(R^a)-C(=O)OR^a$,
(p) $-(CH_2)_{1-3}N(R^a)-C(=O)R^a$,
(q) $-N(R^a)_2$,
(r) $-(CH_2)_{1-3}N(R^a)_2$,
(s) $-(CH_2)_{0-3}C(=O)R^t$,
(t) $-R^t$,
(u) $-N(R^a)R^t$, and
(v) $-(CH_2)_{1-3}R^t$; or

(6) an 8- to 10- membered heterobicyclic ring containing from 1 to 4 heteroatoms independently selected from oxygen, nitrogen and sulfur, wherein the heterobicyclic ring is saturated or unsaturated, and is unsubstituted or substituted with from 1 to 5 substituents independently selected from:

(a) halogen,
(b) C_{1-6} alkyl,
(c) -O-C_{1-6} alkyl,
(d) C_{1-6} fluoroalkyl,
(e) -O-C_{1-6} fluoroalkyl,
(f) -CN,
(g) =O, and
(h) -OH;

R^t is naphthyl or a 5- or 6-membered heteromonocylic ring containing from 1 to 4 nitrogen atoms, wherein the heteromonocyclic ring is saturated or unsaturated, and wherein the naphthyl or the heteromonocyclic ring is unsubstituted or substituted with 1 or 2 substituents independently selected from halogen, oxo, C_{1-4} alkyl, and -O-C_{1-4} alkyl; and

n is an integer equal to 0, 1 or 2;

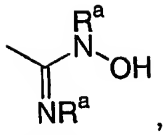
or a pharmaceutically acceptable salt thereof.

A twelfth embodiment of the present invention is a compound of Formula (II), wherein

Z^1 is CH;

Q^2 is

(1) -H,
(2) -C_{1-4} alkyl,
(3) -$(CH_2)_{0-2}CF_3$,
(4) -O-C_{1-4} alkyl,
(5) -O-$(CH_2)_{0-2}CF_3$,
(6) halo selected from -F, -Cl and -Br,
(7) -CN,
(8) -$(CH_2)_{1-3}OR^a$,
(9) -$(CH_2)_{0-2}C(=O)R^a$,
(10) -$(CH_2)_{0-2}CO_2R^a$,
(11) -$(CH_2)_{0-2}SR^a$,
(12) -$N(R^a)_2$,
(13) -$(CH_2)_{1-3}N(R^a)_2$,
(14) -$(CH_2)_{0-2}C(=O)N(R^a)_2$,
(15) -G-$(CH_2)_{1-2}$-$C(=O)N(R^a)_2$, wherein G is O, S, $N(R^a)$, or $N(SO_2R^a)$,
(16) -$N(R^a)$-$C(R^a)$=O,
(17) -$(CH_2)_{1-2}$-$N(R^a)$-$C(R^a)$=O,
(18) -C(=O)-$N(R^a)$-$(CH_2)_{1-3}$-$[C(=O)]_{0-1}$-$N(R^a)_2$,
(19) -C(=O)-$N(R^a)$-$(CH_2)_{1-2}$H substituted with 1 or 2 -OR^a,
(20) -SO_2R^a,
(21) -$N(R^a)SO_2R^a$,
(22) -CH=CH-$(CH_2)_{0-1}$-C(=O)-$N(R^a)_2$,
(23) $—C{\equiv}C—CH_2OR^a$,
(24) $—C{\equiv}C—CH_2SR^a$,
(25) $—C{\equiv}C—CH_2SO_2R^a$,

(26)  ,

(27) -N(R^a)-(CH_2)$_{1-4}$SR^a,

(28) -N(R^a)-(CH_2)$_{1-4}$OR^a,

(29) -N(R^a)-(CH_2)$_{1-4}$-N(R^a)$_2$,

(30) -N(R^a)-(CH_2)$_{1-4}$N(R^a)-C(R^a)=O,

(31) -N(R^a)-(CH_2)$_{0-2}$-[C(=O)]$_{1-2}$N(R^a)$_2$,

(32) -N(R^a)-(CH_2)$_{1-4}$-CO_2R^a,

(33) -N(R^a)C(=O)N(R^a)-(CH_2)$_{1-4}$-C(=O)N(R^a)$_2$,

(34) -N(R^a)C(=O)-(CH_2)$_{1-4}$-N(R^a)$_2$,

(35) -N(R^a)-SO_2-N(R^a)$_2$,

(36) -R^k,

(37) -(CH_2)$_{1-4}$$R^k$,

(38) —C≡C—CH_2R^k ,

(39) -O-R^k,

(40) -S(O)$_n$-R^k,

(41) -N(R^c)-R^k,

(42) -N(R^c)-(CH_2)$_{1-4}$H substituted with one or two R^k groups,

(43) -N(R^c)-(CH_2)$_{1-4}$OR^k,

(44) -C(=O)-R^k,

(45) -C(=O)N(R^a)-R^k,

(46) -N(R^a)C(=O)-R^k, or

(47) -C(=O)N(R^a)-(CH_2)$_{1-4}$$R^k$; and

(48) -N(R^a)-S(O)$_n$$R^k$;

Q^4 is -H;

each of R^1 and R^2 is independently:

(1) -H,

(2) -C_{1-4} alkyl,

(3) -(CH_2)$_{0-2}$$CF_3$,

(4) -O-C_{1-4} alkyl,

(5) -O-(CH_2)$_{0-2}$$CF_3$,

(6) -OH,
(7) halo selected from -F, -Cl and -Br,
(8) -CN,
(9) $-(CH_2)_{1-3}OR^a$,
(10) $-(CH_2)_{0-2}C(=O)R^a$,
(11) $-(CH_2)_{0-2}CO_2R^a$,
(12) $-(CH_2)_{0-2}SR^a$,
(13) $-N(R^a)_2$,
(14) $-(CH_2)_{1-3}N(R^a)_2$,
(15) $-(CH_2)_{0-2}C(=O)N(R^a)_2$,
(16) $-C_{1-4}$ alkyl-$N(R^a)$-$C(R^a)$=O,
(17) $-SO_2R^a$,
(18) $-N(R^a)SO_2R^a$,
(19) $-O-(CH_2)_{1-4}OR^a$,
(20) $-O-(CH_2)_{1-4}SR^a$,
(21) $-O-(CH_2)_{1-4}NH-CO_2R^a$,
(22) $-O-(CH_2)_{2-4}N(R^a)_2$,
(23) $-N(R^a)-(CH_2)_{1-4}SR^a$,
(24) $-N(R^a)-(CH_2)_{1-4}OR^a$,
(25) $-N(R^a)-(CH_2)_{1-4}N(R^a)_2$,
(26) $-N(R^a)-(CH_2)_{1-4}N(R^a)-C(R^a)=O$,
(27) $-R^k$,
(28) $-(CH_2)_{1-4}$H substituted with 1 or 2 R^k groups,
(29) $-O-R^k$,
(30) $-O-(CH_2)_{1-4}R^k$,
(31) $-S(O)_n-R^k$,
(32) $-S(O)_n-(CH_2)_{1-4}R^k$,
(33) $-O-(CH_2)_{1-4}OR^k$,
(34) $-O-(CH_2)_{1-4}-O-(CH_2)_{1-4}R^k$,
(35) $-O-(CH_2)_{1-4}SR^k$, or
(36) $-(CH_2)_{0-4}N(R^b)(R^k)$;

each of R^3 and R^4 is independently
(1) -H,

(2) halo selected from -F, -Cl and -Br,
(3) -CN,
(4) -OH,
(5) C_{1-4} alkyl,
(6) $-(CH_2)_{0-2}CF_3$,
(7) $-O-C_{1-4}$ alkyl, or
(8) $-O(CH_2)_{0-2}CF_3$; and

R^5 is

(1) -H,
(2) $-C_{1-4}$ alkyl,
(3) $-(CH_2)_{1-4}N(R^a)_2$,
(4) $-(CH_2)_{1-4}CO_2R^a$,
(5) phenyl optionally substituted with from 1 to 3 substituents independently selected from halogen, C_{1-4} alkyl, $-(CH_2)_{0-2}CF_3$, $-O-C_{1-4}$ alkyl, $-O(CH_2)_{0-2}CF_3$, $-S-C_{1-4}$ alkyl, -CN, and -OH, or
(6) $-(CH_2)_{1-4}$-phenyl;

and all other variables are as defined in either the tenth embodiment or the eleventh embodiment;

or a pharmaceutically acceptable salt thereof.

A thirteenth embodiment of the present invention is a compound of Formula II, wherein:

Z^1 is CH;

Q^2 is

(1) -H,
(2) $-C_{1-4}$ alkyl,
(3) $-(CH_2)_{0-2}CF_3$,
(4) $-O-C_{1-4}$ alkyl,

(5) -O-$(CH_2)_{0-2}CF_3$,
(6) halo selected from -F, -Cl and -Br,
(7) -CN,
(8) -$(CH_2)_{1-3}OR^a$,
(9) -$(CH_2)_{0-2}C(=O)R^a$,
(10) -$(CH_2)_{0-2}CO_2R^a$,
(11) -$(CH_2)_{0-2}SR^a$,
(12) -$N(R^a)_2$,
(13) -$(CH_2)_{1-3}N(R^a)_2$,
(14) -$(CH_2)_{0-2}C(=O)N(R^a)_2$,
(15) -SO_2R^a,
(16) -$N(R^a)SO_2R^a$,
(17) $—C\equiv C—CH_2OR^a$,
(18) -$N(R^a)$-$(CH_2)_{1-4}SR^a$,
(19) -$N(R^a)$-$(CH_2)_{1-4}OR^a$,
(20) -$N(R^a)$-$(CH_2)_{1-4}$-$N(R^a)_2$,
(21) -$N(R^a)$-$(CH_2)_{1-4}N(R^a)$-$C(R^a)$=O,
(22) -R^k,
(23) -$(CH_2)_{1-4}R^k$,
(24) $—C\equiv C—CH_2R^k$,
(25) -O-R^k,
(26) -$S(O)_n$-R^k,
(27) -$N(R^c)$-R^k,
(28) -$N(R^c)$-$(CH_2)_{1-4}$H substituted with one or two R^k groups,
(29) -$N(R^c)$-$(CH_2)_{1-4}OR^k$,
(30) -C(=O)N-$(CH_2)_{1-4}R^k$,
(31) $—C\equiv C—CH_2SR^a$, or
(32) $—C\equiv C—CH_2SO_2R^a$;

Q^4 is -H;

each of R^1 and R^2 is independently:

(1) -H,
(2) -C_{1-4} alkyl,

(3) -$(CH_2)_{0-2}CF_3$,
(4) -O-C_{1-4} alkyl,
(5) -O-$(CH_2)_{0-2}CF_3$,
(6) -OH,
(7) halo selected from -F, -Cl and -Br,
(8) -CN,
(9) -$(CH_2)_{1-3}OR^a$,
(10) -$(CH_2)_{0-2}C(=O)R^a$,
(11) -$(CH_2)_{0-2}CO_2R^a$,
(12) -$(CH_2)_{0-2}SR^a$,
(13) -$N(R^a)_2$,
(14) -$(CH_2)_{1-3}N(R^a)_2$,
(15) -$(CH_2)_{0-2}C(=O)N(R^a)_2$,
(16) -C_{1-4} alkyl-$N(R^a)$-$C(R^a)$=O,
(17) -SO_2R^a,
(18) -$N(R^a)SO_2R^a$,
(19) -O-$(CH_2)_{1-4}OR^a$,
(20) -O-$(CH_2)_{1-4}SR^a$,
(21) -O-$(CH_2)_{1-4}NH$-CO_2R^a,
(22) -O-$(CH_2)_{2-4}N(R^a)_2$,
(23) -$N(R^a)$-$(CH_2)_{1-4}SR^a$,
(24) -$N(R^a)$-$(CH_2)_{1-4}OR^a$,
(25) -$N(R^a)$-$(CH_2)_{1-4}N(R^a)_2$,
(26) -$N(R^a)$-$(CH_2)_{1-4}N(R^a)$-$C(R^a)$=O,
(27) -R^k,
(28) -$(CH_2)_{1-4}$H substituted with 1 or 2 R^k groups,
(29) -O-R^k,
(30) -O-$(CH_2)_{1-4}R^k$,
(31) -$S(O)_n$-R^k,
(32) -$S(O)_n$-$(CH_2)_{1-4}R^k$,
(33) -O-$(CH_2)_{1-4}OR^k$,
(34) -O-$(CH_2)_{1-4}$-O-$(CH_2)_{1-4}R^k$,
(35) -O-$(CH_2)_{1-4}SR^k$, or
(36) -$(CH_2)_{0-4}N(R^b)(R^k)$;

each of R^3 and R^4 is independently

(1) -H,
(2) halo selected from -F, -Cl and -Br,
(3) -CN,
(4) -OH,
(5) C_{1-4} alkyl,
(6) $-(CH_2)_{0-2}CF_3$,
(7) $-O-C_{1-4}$ alkyl, or
(8) $-O(CH_2)_{0-2}CF_3$,

R^5 is

(1) -H,
(2) $-C_{1-4}$ alkyl,
(3) $-(CH_2)_{1-4}N(R^a)_2$,
(4) $-(CH_2)_{1-4}CO_2R^a$,
(5) phenyl optionally substituted with from 1 to 3 substituents independently selected from halogen, C_{1-4} alkyl, $-(CH_2)_{0-2}CF_3$, $-O-C_{1-4}$ alkyl, $-O(CH_2)_{0-2}CF_3$, $-S-C_{1-4}$ alkyl, -CN, and -OH, or
(6) $-(CH_2)_{1-4}$-phenyl;

each R^a is independently -H or $-C_{1-4}$ alkyl;

each R^b is independently:

(1) -H,
(2) $-C_{1-4}$ alkyl,
(3) $-CF_3$,
(4) $-R^k$, or
(5) $-(CH_2)_{1-4}-R^k$;

each R^c is independently

(1) -H,
(2) $-C_{1-4}$ alkyl,

(3) $-(CH_2)_{1-4}N(R^a)_2$, or

(4) $-(CH_2)_{1-4}$-phenyl, wherein the phenyl is optionally substituted with 1 to 3 substituents independently selected from halogen, C_{1-4} alkyl, C_{1-4} fluoroalkyl, $-O-C_{1-4}$ alkyl, $-O-C_{1-4}$ fluoroalkyl, $-S-C_{1-4}$ alkyl, -CN, and -OH; and

each R^k is independently:

(1) aryl selected from phenyl and naphthyl, wherein aryl is unsubstituted or substituted with from 1 to 4 substituents independently selected from:

(a) halogen,
(b) C_{1-4} alkyl,
(c) C_{1-4} fluoroalkyl,
(d) $-O-C_{1-4}$ alkyl,
(e) $-O-C_{1-4}$ fluoroalkyl,
(f) phenyl,
(g) $-S-C_{1-4}$ alkyl,
(h) -CN,
(i) -OH,
(j) phenyloxy, unsubstituted or substituted with from 1 to 3 substituents independently selected from:
  (i) halogen,
  (ii) C_{1-4} alkyl,
  (iii) C_{1-4} fluoroalkyl, and
  (iv) -OH,
(k) $-N(R^a)_2$,
(l) $-C_{1-4}$ alkyl-$N(R^a)_2$,
(m) $-R^t$,
(p) $-(CH_2)_{0-3}C(=O)N(R^a)_2$, and
(q) $-(CH_2)_{0-3}C(=O)R^a$;

(2) $-C_{3-6}$ cycloalkyl, unsubstituted or substituted with from 1 to 3 substituents independently selected from:

(a) halogen,
(b) C_{1-4} alkyl,
(c) $-O-C_{1-4}$ alkyl,

(d) C_{1-4} fluoroalkyl,
(e) -O-C_{1-4} fluoroalkyl,
(f) -CN,
(h) phenyl, and
(j) -OH;

(3) -C_{3-6} cycloalkyl fused with a phenyl ring, unsubstituted or substituted with from 1 to 4 substituents independently selected from:
(a) halogen,
(b) C_{1-4} alkyl,
(c) -O-C_{1-4} alkyl,
(d) C_{1-4} fluoroalkyl,
(e) -O-C_{1-4} fluoroalkyl,
(f) -CN, and
(g) -OH;

(4) a 5- or 6- membered heteroaromatic ring selected from thienyl, pyridyl, imidazolyl, pyrrolyl, pyrazolyl, thiazolyl, isothiazolyl, oxazolyl, isooxazolyl, pyrazinyl, pyirimidinyl, triazolyl, tetrazolyl,furanyl, and pyridazinyl, wherein the heteroaromatic ring is unsubstituted or substituted on nitrogen or carbon with from 1 to 4 substituents independently selected from:
(a) halogen,
(b) C_{1-4} alkyl,
(c) C_{1-4} fluoroalkyl,
(d) -O-C_{1-4} alkyl,
(e) -O-C_{1-4} fluoroalkyl,
(f) phenyl,
(g) -S-C_{1-4} alkyl,
(h) -CN,
(i) -OH,
(j) phenyloxy, unsubstituted or substituted with from 1 to 3 substituents independently selected from:
(i) halogen,
(ii) C_{1-4} alkyl,
(iii) C_{1-4} fluoroalkyl, and
(iv) -OH,

(k) $-N(R^a)_2$,
(l) $-C_{1-4}$ alkyl-$N(R^a)_2$,
(m) $-R^t$,
(n) oxo,
(o) $-(CH_2)_{0-3}C(=O)N(R^a)_2$, and
(p) $-(CH_2)_{0-3}C(=O)R^a$;

(5) a 5- or 6- membered saturated heterocyclic ring selected from piperidinyl, morpholinyl, thiomorpholinyl, thiazolidinyl, isothiazolidinyl, oxazolidinyl, isooxazolidinyl, pyrrolidinyl, imidazolidinyl, piperazinyl, tetrahydrofuranyl, and pyrazolidinyl, wherein the heterocyclic ring is unsubstituted or substituted with from 1 to 3 substituents independently selected from:

(a) halogen,
(b) C_{1-4} alkyl,
(c) -O-C_{1-4} alkyl,
(d) C_{1-4} fluoroalkyl,
(e) -O-C_{1-4} fluoroalkyl,
(f) -CN,
(g) =O,
(h) phenyl,
(i) benzyl,
(j) phenylethyl,
(k) -OH,
(l) $-(CH_2)_{0-3}C(=O)N(R^a)_2$,
(m) $-(CH_2)_{0-3}C(=O)R^a$,
(n) $N(R^a)$-$C(=O)R^a$,
(o) $N(R^a)$-$C(=O)OR^a$,
(p) $(CH_2)_{1-3}N(R^a)$-$C(=O)R^a$,
(q) $N(R^a)_2$,
(r) $(CH_2)_{1-3}N(R^a)_2$,
(s) $-(CH_2)_{0-3}C(=O)R^t$,
(t) $-R^t$,
(u) $-N(R^a)R^t$, and
(v) $-(CH_2)_{1-3}R^t$; or

(6) an 8- to 10- membered heterobicyclic ring selected from indolyl, benzotriazolyl, benzoimidazolyl, imidazo[4,5-b]pyridinyl, dihydroimidazo[4,5-b]pyridinyl, pyrazolo[4,3-c]pyridinyl, dihydropyrazolo[4,3-c]pyridinyl, tetrahydropyrazolo[4,3-c]pyridinyl, pyrrolo[1,2-a]pyrazinyl, dihydropyrrolo[1,2-a]pyrazinyl, tetrahydropyrrolo[1,2-a]pyrazinyl, octahydropyrrolo[1,2-a]pyrazinyl, isoindolyl, indazolyl, indolinyl, isoindolinyl, quinolinyl, isoquinolinyl, quinoxalinyl, quinazolinyl, cinnolinyl, chromanyl, and isochromanyl, wherein the bicyclic ring is unsubstituted or substituted with 1 or 2 substituents independently selected from:

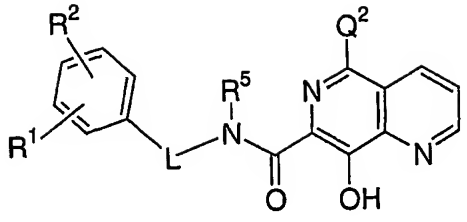
(a) halogen,
(b) C_{1-4} alkyl,
(c) -O-C_{1-4} alkyl,
(d) C_{1-4} fluoroalkyl,
(e) -O-C_{1-4} fluoroalkyl,
(f) -CN,
(g) =O, and
(h) -OH;

R^t is naphthyl or a 5- or 6-membered heteromonocylic ring selected from pyrrolidinyl, pyrazolidinyl, imidazolinyl, piperidinyl, piperazinyl, pyrrolyl, pyridyl, imidazolyl, pyrazolyl, triazolyl, tetrazolyl, pyrazinyl, pyrimidinyl, and pyradizinyl; and wherein the naphthyl or the heteromonocyclic ring is unsubstituted or substituted with 1 or 2 substituents independently selected from halogen, oxo, C_{1-4} alkyl, and -O-C_{1-4} alkyl;

and all other variables are as defined in the eleventh embodiment;

or a pharmaceutically acceptable salt thereof.

A fourteenth embodiment of the present invention is compounds of Formula (III):



(III);

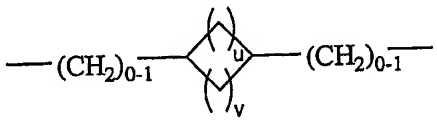
wherein each of the variables is as defined in any one of the tenth, eleventh, twelfth or thirteenth embodiments; or, alternatively, as originally defined or as defined in any other preceding embodiment containing any one or more of the variables; or a pharmaceutically acceptable salt thereof.

A fifteenth embodiment of the present invention is compounds of Formula (III), wherein:

L is

(i) a single bond;

(ii) $-(CH_2)_{1-3}-$, which is optionally substituted with 1 or 2 substituents independently selected from the group consisting of -OH, methyl, ethyl, $-CO_2CH_3$, $-CO_2CH_2$-phenyl, phenyl, benzyl, $-(CH_2)_{1-2}OH$, -CH(OH)-phenyl, and $-CH(NH_2)$-phenyl; or

(iii)  , wherein u and v are each integers having a value of from 0 to 3, provided that the sum of u + v is 1, 2, 3 or 4;

Q^2 is

(1) -H,

(2) methyl,

(3) ethyl,

(4) CF_3,

(5) methoxy,

(6) ethoxy
(7) $-OCF_3$
(8) halo selected from -F, -Cl and -Br,
(9) -CN,
(10) $-CH_2OH$,
(11) $-CH_2OCH_3$
(12) $-(CH_2)_{0-2}CO_2CH_3$,
(13) $-SR^a$,
(14) $-N(R^a)_2$,
(15) $-SO_2R^a$,
(16) $-C\equiv C-CH_2OR^a$,
(17) $-N(R^a)-(CH_2)_{1-3}SR^a$,
(18) $-N(R^a)-(CH_2)_{1-3}OR^a$,
(19) $-N(R^a)-(CH_2)_{1-3}N(R^a)_2$,
(20) $-N(R^a)-(CH_2)_{1-3}N(R^a)-C(R^a)=O$,
(21) $-R^k$,
(22) $-(CH_2)_{1-4}R^k$,
(23) $-C\equiv C-CH_2R^k$,
(24) $-O-R^k$,
(25) $-S-R^k$,
(26) $-SO_2-R^k$,
(27) $-N(R^c)-R^k$,
(28) $-N(R^c)-(CH_2)_{1-4}H$ substituted with one or two R^k groups,
(29) $-N(R^c)-(CH_2)_{1-4}OR^k$,
(30) $-C(=O)N-(CH_2)_{1-4}R^k$,
(31) $-C\equiv C-CH_2SR^a$, or
(32) $-C\equiv C-CH_2SO_2R^a$;

each of R^1 and R^2 is independently:

(1) -H,
(2) methyl,
(3) ethyl,
(4) CF_3,
(5) methoxy,

(6) ethoxy
(7) $-OCF_3$
(8) halo selected from -F, -Cl and -Br,
(9) -CN,
(10) $-CH_2OR^a$,
(11) $-CO_2R^a$,
(12) $-SR^a$,
(13) $-N(R^a)_2$,
(14) $-(CH_2)_{1-3}N(R^a)_2$,
(15) $-SO_2R^a$,
(16) $-(CH_2)_{1-2}N(R^a)-C(R^a)=O$,
(17) $-R^k$,
(18) $-(CH_2)_{1-3}H$ substituted with 1 or 2 R^k groups,
(19) $-O-R^k$, or
(20) $-O-(CH_2)_{1-3}R^k$;

R^5 is

(1) -H,
(2) methyl,
(3) $-(CH_2)_{1-2}N(R^a)_2$,
(4) $-(CH_2)_{1-2}CO_2CH_3$, or
(5) $-(CH_2)_{1-2}CO_2CH_2CH_3$;
(6) phenyl, or
(7) benzyl;

each R^a is independently -H or $-C_{1-4}$ alkyl;

each R^c is independently -H, $-C_{1-4}$ alkyl, or $-(CH_2)_{1-3}N(R^a)_2$;

each R^k is independently:

(1) phenyl which is unsubstituted or substituted with from 1 to 4 substituents independently selected from:

(a) halogen selected from -F, -Cl, and -Br,
(b) methyl,

(c) $-CF_3$,
(d) methoxy,
(e) $-OCF_3$,
(f) phenyl,
(g) $-S-CH_3$,
(h) -CN,
(i) -OH,
(j) phenyloxy, unsubstituted or substituted with from 1 to 3 substituents independently selected from:
(i) halogen selected from -F, -Cl, and -Br,
(ii) methyl,
(iii) $-CF_3$, and
(iv) -OH,
(k) $-N(R^a)_2$,
(l) $-(CH_2)_{1-3}N(R^a)_2$,
(m) $-R^t$,
(p) $-(CH_2)_{0-3}C(=O)N(R^a)_2$, and
(q) $-(CH_2)_{0-3}C(=O)R^a$;

(2) $-C_{3-6}$ cycloalkyl, unsubstituted or substituted with from 1 to 3 substituents independently selected from:
(a) halogen selected from -F, -Cl, and -Br,
(b) methyl,
(c) $-CF_3$,
(d) methoxy,
(e) $-OCF_3$,
(f) -CN,
(h) phenyl, and
(j) -OH;

(3) a 5- or 6- membered heteroaromatic ring selected from thienyl, pyridyl, imidazolyl, pyrrolyl, pyrazolyl, thiazolyl, isothiazolyl, oxazolyl, isooxazolyl, pyrazinyl, pyirimidinyl, triazolyl, tetrazolyl, furanyl, and pyridazinyl, wherein the heteroaromatic ring is unsubstituted or substituted on nitrogen or carbon with 1 or 2 substituents independently selected from:
(a) halogen selected from -F, -Cl, and -Br,

(b) methyl,
(c) $-CF_3$,
(d) methoxy,
(e) $-OCF_3$,
(f) phenyl,
(g) $-S-C_{1-6}$ alkyl,
(h) -CN,
(i) -OH,
(j) phenyloxy, unsubstituted or substituted with from 1 to 3 substituents independently selected from:
(i) halogen selected from -F, -Cl, and -Br,
(ii) methyl,
(iii) $-CF_3$, and
(iv) -OH,
(k) $-N(R^a)_2$,
(l) $-C_{1-6}$ alkyl-$N(R^a)_2$,
(m) $-R^t$,
(n) oxo,
(o) $-(CH_2)_{0-3}C(=O)N(R^a)_2$, and
(p) $-(CH_2)_{0-3}C(=O)R^a$;

(4) a 5- or 6- membered saturated heterocyclic ring selected from piperidinyl, morpholinyl, thiomorpholinyl, thiazolidinyl, isothiazolidinyl, oxazolidinyl, isooxazolidinyl, pyrrolidinyl, imidazolidinyl, piperazinyl, tetrahydrofuranyl, and pyrazolidinyl, wherein the heterocyclic ring is unsubstituted or substituted with 1 or 2 substituents independently selected from:
(a) halogen selected from -F, -Cl, and -Br,
(b) methyl,
(c) $-CF_3$,
(d) methoxy,
(e) $-OCF_3$,
(f) -CN,
(g) =O,
(h) phenyl,
(i) benzyl,

(j) phenylethyl,
(k) -OH,
(l) $-(CH_2)_{0-3}C(=O)N(R^a)_2$,
(m) $-(CH_2)_{0-3}C(=O)R^a$,
(n) $N(R^a)-C(=O)R^a$,
(o) $N(R^a)-C(=O)OR^a$,
(p) $(CH_2)_{1-3}N(R^a)-C(=O)R^a$,
(q) $N(R^a)_2$,
(r) $(CH_2)_{1-3}N(R^a)_2$,
(s) $-(CH_2)_{0-3}C(=O)R^t$,
(t) $-R^t$,
(u) $-N(R^a)R^t$, and
(v) $-(CH_2)_{1-3}R^t$; and

(5) an 8- to 10- membered heterobicyclic ring selected from indolyl, benzotriazolyl, benzoimidazolyl, imidazo[4,5-b]pyridinyl, dihydroimidazo[4,5-b]pyridinyl, pyrazolo[4,3-c]pyridinyl, dihydropyrazolo[4,3-c]pyridinyl, tetrahydropyrazolo[4,3-c]pyridinyl, pyrrolo[1,2-a]pyrazinyl, dihydropyrrolo[1,2-a]pyrazinyl, tetrahydropyrrolo[1,2-a]pyrazinyl, octahydropyrrolo[1,2-a]pyrazinyl, isoindolyl, indazolyl, indolinyl, isoindolinyl, quinolinyl, isoquinolinyl, quinoxalinyl, quinazolinyl, cinnolinyl, chromanyl, and isochromanyl, wherein the bicyclic ring is unsubstituted or substituted with 1 or 2 substituents independently selected from:

(a) halogen selected from -F, -Cl, and -Br,
(b) methyl,
(c) $-CF_3$,
(d) methoxy,
(e) $-OCF_3$,
(f) -CN,
(g) =O, and
(h) -OH;

R^t is selected from pyrrolidinyl, pyrazolidinyl, imidazolinyl, piperidinyl, piperazinyl, pyrrolyl, pyridyl, imidazolyl, pyrazolyl, triazolyl, tetrazolyl, pyrazinyl, pyrimidinyl,

and pyradizinyl; any one of which is unsubstituted or substituted with 1 or 2 substituents independently selected from -F, -Cl, -Br, oxo, methyl, and methoxy;

or a pharmaceutically acceptable salt thereof.

A sixteenth embodiment of the present invention is a compound of Formula (III), wherein

L is

(i) a single bond;

(ii) $-(CH_2)_{1-3}-$, which is optionally substituted with 1 or 2 substituents independently selected from the group consisting of -F, -Cl, -Br, -OH, methyl, ethyl, $-CO_2CH_3$, $-CO_2CH_2$-phenyl, phenyl, benzyl, $-(CH_2)_{1-2}OH$, -CH(OH)-phenyl, and $-CH(NH_2)$-phenyl; or

(iii)  , wherein u and v are each integers having a value of from 0 to 3, provided that the sum of u + v is 1, 2, 3 or 4;

each of R^1 and R^2 is independently:

(1) -H,

(2) methyl,

(3) ethyl,

(4) CF_3,

(5) methoxy,

(6) ethoxy

(7) $-OCF_3$

(8) halo selected from -F, -Cl and -Br,

(9) -CN,

(10) $-CH_2OR^a$,

(11) $-CO_2R^a$,

(12) $-SR^a$,

(13) $-N(R^a)_2$,
(14) $-(CH_2)_{1-3}N(R^a)_2$,
(15) $-SO_2R^a$,
(16) $-(CH_2)_{1-2}N(R^a)-C(R^a)=O$,
(17) $-R^k$,
(18) $-(CH_2)_{1-3}H$ substituted with 1 or 2 R^k groups,
(19) $-O-R^k$, or
(20) $-O-(CH_2)_{1-3}R^k$;

R^5 is

(1) -H,
(2) methyl,
(3) $-(CH_2)_{1-2}N(R^a)_2$,
(4) $-(CH_2)_{1-2}CO_2CH_3$, or
(5) $-(CH_2)_{1-2}CO_2CH_2CH_3$;
(6) phenyl, or
(7) benzyl;

each R^a is independently -H or $-C_{1-4}$ alkyl;

each R^c is independently

(1) -H,
(2) $-C_{1-4}$ alkyl,
(3) $-(CH_2)_{1-4}N(R^a)_2$, or
(4) $-(CH_2)_{1-4}$-phenyl, wherein the phenyl is optionally substituted with 1 to 3 substituents independently selected from halogen, C_{1-4} alkyl, C_{1-4} fluoroalkyl, $-O-C_{1-4}$ alkyl, $-O-C_{1-4}$ fluoroalkyl, $-S-C_{1-4}$ alkyl, -CN, and -OH; and

each R^k is independently:

(1) aryl selected from phenyl and naphthyl, wherein aryl is unsubstituted or substituted with from 1 to 4 substituents independently selected from:
(a) halogen,
(b) C_{1-4} alkyl,

(c) C_{1-4} fluoroalkyl,
(d) -O-C_{1-4} alkyl,
(e) -O-C_{1-4} fluoroalkyl,
(f) phenyl,
(g) -S-C_{1-4} alkyl,
(h) -CN,
(i) -OH,
(j) phenyloxy, unsubstituted or substituted with from 1 to 3 substituents independently selected from:
(i) halogen,
(ii) C_{1-4} alkyl,
(iii) C_{1-4} fluoroalkyl, and
(iv) -OH,
(k) -$N(R^a)_2$,
(l) -C_{1-4} alkyl-$N(R^a)_2$,
(m) -R^t,
(p) -$(CH_2)_{0-3}C(=O)N(R^a)_2$, and
(q) -$(CH_2)_{0-3}C(=O)R^a$;

(2) -C_{3-6} cycloalkyl, unsubstituted or substituted with from 1 to 3 substituents independently selected from:
(a) halogen,
(b) C_{1-4} alkyl,
(c) -O-C_{1-4} alkyl,
(d) C_{1-4} fluoroalkyl,
(e) -O-C_{1-4} fluoroalkyl,
(f) -CN,
(h) phenyl, and
(j) -OH;

(3) -C_{3-6} cycloalkyl fused with a phenyl ring, unsubstituted or substituted with from 1 to 4 substituents independently selected from:
(a) halogen,
(b) C_{1-4} alkyl,
(c) -O-C_{1-4} alkyl,
(d) C_{1-4} fluoroalkyl,

(e) -O-C_{1-4} fluoroalkyl,

(f) -CN, and

(g) -OH;

(4) a 5- or 6- membered heteroaromatic ring selected from thienyl, pyridyl, imidazolyl, pyrrolyl, pyrazolyl, thiazolyl, isothiazolyl, oxazolyl, isooxazolyl, pyrazinyl, pyrimidinyl, triazolyl, tetrazolyl,furanyl, and pyridazinyl, wherein the heteroaromatic ring is unsubstituted or substituted on nitrogen or carbon with from 1 to 4 substituents independently selected from:

(a) halogen,

(b) C_{1-4} alkyl,

(c) C_{1-4} fluoroalkyl,

(d) -O-C_{1-4} alkyl,

(e) -O-C_{1-4} fluoroalkyl,

(f) phenyl,

(g) -S-C_{1-4} alkyl,

(h) -CN,

(i) -OH,

(j) phenyloxy, unsubstituted or substituted with from 1 to 3 substituents independently selected from:

(i) halogen,

(ii) C_{1-4} alkyl,

(iii) C_{1-4} fluoroalkyl, and

(iv) -OH,

(k) -$N(R^a)_2$,

(l) -C_{1-4} alkyl-$N(R^a)_2$,

(m) -R^t,

(n) oxo,

(o) -$(CH_2)_{0-3}C(=O)N(R^a)_2$, and

(p) -$(CH_2)_{0-3}C(=O)R^a$;

(5) a 5- or 6- or 7- membered saturated heterocyclic ring selected from piperidinyl, morpholinyl, thiomorpholinyl, thiazolidinyl, isothiazolidinyl, oxazolidinyl, isooxazolidinyl, pyrrolidinyl, imidazolidinyl, piperazinyl, tetrahydrofuranyl, pyrazolidinyl, hexahydropyrimidinyl, thiazinanyl, thiazepanyl, azepanyl, thiadiazepanyl, dithiazepanyl, diazepanyl, and thiadiazinanyl, and wherein

the heterocyclic ring is unsubstituted or substituted with from 1 to 4 substituents independently selected from:

(a) halogen,
(b) C_{1-6} alkyl,
(c) -O-C_{1-6} alkyl,
(d) C_{1-6} fluoroalkyl,
(e) -O-C_{1-6} fluoroalkyl,
(f) -CN,
(g) oxo,
(h) phenyl
(i) benzyl,
(j) phenylethyl,
(k) -OH,
(l) $-(CH_2)_{0-3}C(=O)N(R^a)_2$,
(m) $-(CH_2)_{0-3}C(=O)R^a$,
(n) $-N(R^a)-C(=O)R^a$,
(o) $-N(R^a)-CO_2R^a$,
(p) $-(CH_2)_{1-3}N(R^a)-C(=O)R^a$,
(q) $-N(R^a)_2$,
(r) $-(CH_2)_{1-3}N(R^a)_2$,
(s) $-(CH_2)_{1-3}-OR^a$,
(t) $-(CH_2)_{0-3}CO_2R^a$,
(u) $-(CH_2)_{0-3}-O-(CH_2)_{1-3}-OR^a$,
(v) $-SO_2R^a$,
(w) $-SO_2N(R^a)_2$,
(x) $-(CH_2)_{0-3}C(=O)O(CH_2)_{1-2}CH=CH_2$,
(y) $-R^t$,
(z) $-(CH_2)_{0-3}C(=O)R^t$,
(aa) $-N(R^a)R^t$, and
(bb) $-(CH_2)_{1-3}R^t$; or

(6) an 8- to 10- membered heterobicyclic ring selected from indolyl, benzotriazolyl, benzoimidazolyl, imidazo[4,5-b]pyridinyl, dihydroimidazo[4,5-b]pyridinyl, pyrazolo[4,3-c]pyridinyl, dihydropyrazolo[4,3-c]pyridinyl, tetrahydropyrazolo[4,3-c]pyridinyl, pyrrolo[1,2-a]pyrazinyl,

dihydropyrrolo[1,2-a]pyrazinyl, tetrahydropyrrolo[1,2-a]pyrazinyl, octahydropyrrolo[1,2-a]pyrazinyl, isoindolyl, indazolyl, indolinyl, isoindolinyl, quinolinyl, isoquinolinyl, quinoxalinyl, quinazolinyl, cinnolinyl, chromanyl, isochromanyl, hexahydropyrazolo[4,3-c]pyridinyl, hexahydropurinyl, hexahydrooxazolo[3,4a]pyrazinyl, and 1,2,3,4-tetrahydro-1,8-naphthyridinyl; and wherein the bicyclic ring is unsubstituted or substituted with from 1 to 3 substituents independently selected from:

(a) halogen,
(b) C_{1-4} alkyl,
(c) -O-C_{1-4} alkyl,
(d) C_{1-4} fluoroalkyl,
(e) -O-C_{1-4} fluoroalkyl,
(f) -CN,
(g) =O, and
(h) -OH;

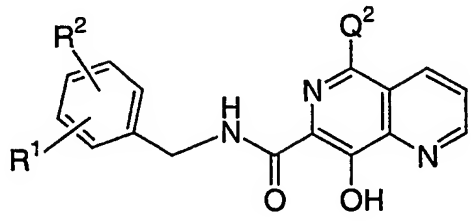
R^t is naphthyl or a 5- or 6-membered heteromonocylic ring selected from pyrrolidinyl, pyrazolidinyl, imidazolinyl, piperidinyl, piperazinyl, pyrrolyl, pyridyl, imidazolyl, pyrazolyl, triazolyl, tetrazolyl, pyrazinyl, pyrimidinyl, and pyradizinyl; and wherein the naphthyl or the heteromonocyclic ring is unsubstituted or substituted with 1 or 2 substituents independently selected from halogen, oxo, C_{1-4} alkyl, and -O-C_{1-4} alkyl;

and Q^2 is as originally defined or as defined in any one of the preceding embodiments;

or a pharmaceutically acceptable salt thereof.

In an aspect of the sixteenth embodiment, the compound of Formula (III) is as just defined above, except that in part (5) of the definition of R^k, the 5- or 6- or 7- membered saturated heterocyclic ring is selected from piperidinyl, morpholinyl, thiomorpholinyl, thiazolidinyl, isothiazolidinyl, oxazolidinyl, isooxazolidinyl, pyrrolidinyl, imidazolidinyl, piperazinyl, tetrahydrofuranyl, pyrazolidinyl, hexahydropyrimidinyl, thiazinanyl, thiazepanyl, and azepanyl.

A first class of the present invention is compounds of Formula (IV):

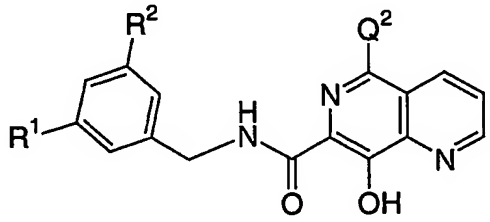


(IV);

wherein each of the variables is as defined in any one of the tenth, eleventh, twelfth, thirteenth, fourteenth, fifteenth, or sixteenth embodiments; or, alternatively, as originally defined, or as defined in any of the other preceding embodiments containing the variables;

or a pharmaceutically acceptable salt thereof.

A first sub-class of the present invention is compounds of Formula (V):



(V);

wherein each of the variables is as defined in either the fifteenth embodiment or the sixteenth embodiment; or, alternatively, as originally defined, or as defined in any of the other preceding embodiments or classes containing the variables;

or a pharmaceutically acceptable salt thereof.

A second sub-class of the present invention is compounds of Formula (V), wherein:

Q^2 is

(1) -H,
(2) methyl,
(3) ethyl,
(4) CF_3,
(5) methoxy,
(6) ethoxy
(7) $-OCF_3$
(8) halo selected from -F, -Cl and -Br,
(9) -CN,
(10) $-CH_2OH$,
(11) $-CH_2OCH_3$
(12) $-SR^a$,
(13) $-N(R^a)_2$,
(14) $-N(H)CH_2CH_2CH_3$,
(15) $-SO_2R^a$,
(16) $-C{\equiv}C-CH_2OR^a$,
(17) $-N(R^a)-(CH_2)_{1-3}SR^a$,
(18) $-N(R^a)-(CH_2)_{1-3}OR^a$,
(19) $-N(R^a)-(CH_2)_{1-3}N(R^a)_2$,
(20) $-N(R^a)-(CH_2)_{1-3}N(R^a)-C(R^a)=O$,
(21) $-R^k$,
(22) $-(CH_2)_{1-4}R^k$,
(23) $-C{\equiv}C-CH_2R^k$,
(24) $-S-R^k$,
(25) $-SO_2-R^k$,
(26) $-N(R^c)-R^k$,
(27) $-N(R^c)-(CH_2)_{1-4}$H substituted with one or two R^k groups,
(28) $-N(R^c)-(CH_2)_{1-4}OR^k$,
(29) $-C{\equiv}C-CH_2SR^a$, or
(30) $-C{\equiv}C-CH_2SO_2R^a$;

R^1 is:

(1) -H,
(2) methyl,

(3) ethyl,
(4) CF_3,
(5) methoxy,
(6) ethoxy
(7) $-OCF_3$
(8) halo selected from -F and -Cl,
(9) -CN,
(10) $-CH_2OR^a$,
(11) $-CO_2R^a$,
(12) $-SR^a$,
(13) $-N(R^a)_2$,
(14) $-(CH_2)_{1-3}N(R^a)_2$,
(15) $-SO_2R^a$,
(16) $-R^k$,
(17) $-(CH_2)_{1-3}R^k$,
(18) $-O-R^k$, or
(19) $-O-(CH_2)_{1-3}R^k$;

R^2 is:

(1) -H,
(2) methyl,
(3) ethyl,
(4) CF_3,
(5) methoxy,
(6) ethoxy
(7) $-OCF_3$
(8) halo selected from -F and -Cl,
(9) -CN,
(10) $-CH_2OR^a$,
(11) $-CO_2R^a$,
(12) $-SR^a$,
(13) $-N(R^a)_2$,
(14) $-(CH_2)_{1-3}N(R^a)_2$, or
(15) $-SO_2R^a$;

each R^a is independently -H or methyl;

each R^c is independently -H, methyl, or $-(CH_2)_{1-3}N(R^a)_2$;

each R^k is independently:

(1) phenyl which is unsubstituted or substituted with from 1 to 2 substituents independently selected from:

(a) halogen selected from -F, -Cl, and -Br,
(b) methyl,
(c) $-CF_3$,
(d) methoxy,
(e) $-OCF_3$,
(f) phenyl,
(g) $-S-CH_3$,
(h) -CN,
(i) -OH,
(j) phenyloxy
(k) $-N(R^a)_2$,
(l) $-(CH_2)_{1-3}N(R^a)_2$,
(m) $-R^t$,
(p) $-(CH_2)_{0-3}C(=O)N(R^a)_2$, and
(q) $-(CH_2)_{0-3}C(=O)R^a$;

(2) $-C_{3-6}$ cycloalkyl;

(3) a 5- or 6- membered heteroaromatic ring selected from thienyl, pyridyl, imidazolyl, pyrrolyl, pyrazolyl, thiazolyl, isothiazolyl, pyrazinyl, pyirimidinyl, triazolyl, and tetrazolyl, wherein the heteroaromatic ring is unsubstituted or substituted on nitrogen or carbon with 1 or 2 substituents independently selected from:

(a) halogen selected from -F, -Cl, and -Br,
(b) methyl,
(c) $-CF_3$,
(d) methoxy,
(e) $-OCF_3$,

(f) -S-C_{1-6} alkyl,
(g) -CN,
(h) -OH,
(i) -$N(R^a)_2$,
(j) -C_{1-6} alkyl-$N(R^a)_2$,
(k) -R^t,
(l) oxo,
(m) -$(CH_2)_{0-3}C(=O)N(R^a)_2$, and
(n) -$(CH_2)_{0-3}C(=O)R^a$;

(4) a 5- or 6- membered saturated heterocyclic ring selected from piperidinyl, morpholinyl, thiomorpholinyl, thiazolidinyl, isothiazolidinyl, pyrrolidinyl, imidazolidinyl and, piperazinyl, wherein the heterocyclic ring is unsubstituted or substituted with 1 or 2 substituents independently selected from:

(a) halogen selected from -F, -Cl, and -Br,
(b) methyl,
(c) -CF_3,
(d) methoxy,
(e) -OCF_3,
(f) -CN,
(g) =O,
(h) phenyl,
(i) benzyl,
(j) phenylethyl,
(k) -OH,
(l) -$(CH_2)_{0-3}C(=O)N(R^a)_2$,
(m) -$(CH_2)_{0-3}C(=O)R^a$,
(n) $N(R^a)$-$C(=O)R^a$,
(o) $N(R^a)$-$C(=O)OR^a$,
(p) $N(R^a)$-$C(=O)OC(CH_3)_3$,
(q) $(CH_2)_{1-3}N(R^a)$-$C(=O)R^a$,
(r) $N(R^a)_2$,
(s) $(CH_2)_{1-3}N(R^a)_2$,
(t) -$(CH_2)_{0-3}C(=O)R^t$,
(u) -R^t,

(v) $-N(R^a)R^t$, and
(w) $-(CH_2)_{1-3}R^t$; and

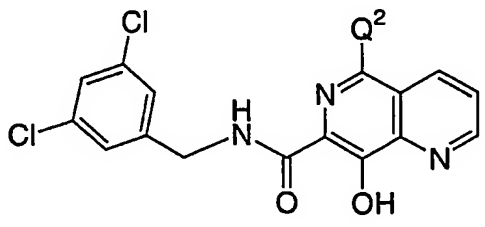
(5) an 8- to 10- membered heterobicyclic ring selected from indolyl, imidazo[4,5-b]pyridinyl, dihydroimidazo[4,5-b]pyridinyl, pyrazolo[4,3-c]pyridinyl, dihydropyrazolo[4,3-c]pyridinyl, tetrahydropyrazolo[4,3-c]pyridinyl, pyrrolo[1,2-a]pyrazinyl, dihydropyrrolo[1,2-a]pyrazinyl, tetrahydropyrrolo[1,2-a]pyrazinyl, octahydropyrrolo[1,2-a]pyrazinyl, isoindolyl, indazolyl, indolinyl, isoindolinyl, quinolinyl, isoquinolinyl, quinoxalinyl, and quinazolinyl, wherein the bicyclic ring is unsubstituted or substituted with 1 or 2 substituents independently selected from:

(a) halogen selected from -F, -Cl, and -Br,
(b) methyl,
(c) $-CF_3$,
(d) methoxy,
(e) $-OCF_3$,
(f) -CN,
(g) =O, and
(h) -OH;

R^t is selected from pyrrolidinyl, pyrazolidinyl, imidazolinyl, piperidinyl, piperazinyl, pyrrolyl, pyridyl, imidazolyl, pyrazolyl, triazolyl, tetrazolyl, pyrazinyl, pyrimidinyl, and pyradizinyl; any one of which is unsubstituted or substituted with 1 or 2 substituents independently selected from -F, -Cl, -Br, oxo, methyl, and methoxy;

or a pharmaceutically acceptable salt thereof.

An aspect of the second sub-class is a compound of Formula (VI):



(VI);

wherein Q^2 is as defined in the second sub-class;

or a pharmaceutically acceptable salt thereof.

A seventeenth embodiment of the present invention is a compound of Formula (IV), wherein

Q^2 is

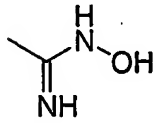
(1) -H,
(2) methyl,
(3) ethyl,
(4) CF_3,
(5) methoxy,
(6) ethoxy
(7) $-OCF_3$
(8) halo selected from -F, -Cl and -Br,
(9) -CN,
(10) $-CH_2OH$,
(11) $-CH_2OCH_3$
(12) $-(CH_2)_{0-2}C(=O)CH_3$,
(13) $-(CH_2)_{0-2}CO_2CH_3$,
(14) $-SR^a$,
(15) $-N(R^a)_2$,
(16) $-(CH_2)_{1-2}N(R^a)_2$,
(17) $-(CH_2)_{0-2}C(=O)N(R^a)_2$,
(18) $-S-CH_2-C(=O)N(R^a)_2$,
(19) $-O-CH_2-C(=O)N(R^a)_2$,
(20) $-N(SO_2R^a)-CH_2-C(=O)N(R^a)_2$,
(21) $-N(R^a)-C(R^a)=O$,
(22) $-C(=O)-N(R^a)-(CH_2)_{1-2}-C(=O)N(R^a)_2$,
(23) $-C(=O)-N(R^a)-(CH_2)_{1-2}OR^a$,
(24) $-C(=O)-N(R^a)-(CH_2)_{1-3}-N(R^a)_2$,
(25) $-SO_2R^a$,
(26) $-N(R^a)SO_2R^a$,

(27) -CH=CH-C(=O)-N(R^a)$_2$,

(28) —C≡C—CH_2OR^a ,

(29) —C≡C—CH_2SR^a ,

(30) —C≡C—$CH_2SO_2R^a$,

(31)  ,

(32) -N(R^a)-(CH_2)$_{1-3}$SR^a,

(33) -N(R^a)-(CH_2)$_{1-3}$OR^a,

(34) -N(R^a)-(CH_2)$_{1-3}$N(R^a)$_2$,

(35) -N(R^a)-(CH_2)$_{1-3}$N(R^a)-C(R^a)=O,

(36) -N(R^a)CH_2-C(=O)N(R^a)$_2$,

(37) -N(R^a)-C(=O)-C(=O)-N(R^a)$_2$,

(38) -N(R^a)-C(=O)-N(R^a)$_2$,

(39) -N(R^a)-(CH_2)$_{1-2}$-CO_2R^a,

(40) -N(R^a)-C(=O)-N(R^a)-(CH_2)$_{1-2}$-C(=O)-N(R^a)$_2$,

(41) -N(R^a)-C(=O)-(CH_2)$_{1-2}$-C(=O)-N(R^a)$_2$,

(42) -N(R^a)-SO_2-N(R^a)$_2$,

(43) -R^k,

(44) -(CH_2)$_{1-4}R^k$,

(45) —C≡C—CH_2R^k ,

(46) -O-R^k,

(47) -S-R^k,

(48) -SO_2-R^k,

(49) -N(R^c)-R^k,

(50) -N(R^c)-(CH_2)$_{1-4}$H substituted with one or two R^k groups,

(51) -N(R^c)-(CH_2)$_{1-4}$OR^k,

(52) -C(=O)-R^k,

(53) -C(=O)N(R^a)-R^k,

(54) -N(R^a)-C(=O)-R^k,

(55) -C(=O)N(R^a)-(CH_2)$_{1-4}R^k$, or

(56) -N(R^a)--SO_2R^k,

each of R^1 and R^2 is independently:

(1) -H,
(2) methyl,
(3) ethyl,
(4) CF_3,
(5) methoxy,
(6) ethoxy
(7) $-OCF_3$
(8) halo selected from -F and -Cl,
(9) -CN,
(10) $-CH_2OR^a$,
(11) $-CO_2R^a$,
(12) $-SR^a$,
(13) $-N(R^a)_2$,
(14) $-(CH_2)_{1-3}N(R^a)_2$,
(15) $-SO_2R^a$,
(16) $-R^k$,
(17) $-(CH_2)_{1-3}R^k$,
(18) $-O-R^k$, or
(19) $-O-(CH_2)_{1-3}R^k$;

each R^a is independently -H or $-C_{1-4}$ alkyl;

each R^c is independently -H, $-C_{1-4}$ alkyl, or $-(CH_2)_{1-3}N(R^a)_2$;

each R^k is independently:

(1) phenyl which is unsubstituted or substituted with from 1 to 4 substituents independently selected from:

(a) halogen selected from -F, -Cl, and -Br,
(b) methyl or ethyl,
(c) $-CF_3$,
(d) methoxy,
(e) $-OCF_3$,
(f) phenyl,
(g) $-S-CH_3$,

(h) -CN,
(i) -OH,
(j) phenyloxy
(k) $-N(R^a)_2$,
(l) $-(CH_2)_{1-3}N(R^a)_2$,
(m) $-R^t$,
(p) $-(CH_2)_{0-3}C(=O)N(R^a)_2$, and
(q) $-(CH_2)_{0-3}C(=O)R^a$;

(2) $-C_{3-6}$ cycloalkyl,

(3) a 5- or 6- membered heteroaromatic ring selected from thienyl, pyridyl, imidazolyl, pyrrolyl, pyrazolyl, thiazolyl, isothiazolyl, oxazolyl, isooxazolyl, pyrazinyl, pyrimidinyl, triazolyl, tetrazolyl, furanyl, and pyridazinyl, wherein the heteroaromatic ring is unsubstituted or substituted on nitrogen or carbon with 1 or 2 substituents independently selected from:

(a) halogen selected from -F, -Cl, and -Br,
(b) methyl or ethyl,
(c) $-CF_3$,
(d) methoxy,
(e) $-OCF_3$,
(f) $-S-C_{1-6}$ alkyl,
(g) -CN,
(h) -OH,
(i) $-N(R^a)_2$,
(j) $-C_{1-6}$ alkyl-$N(R^a)_2$,
(k) $-R^t$,
(l) oxo,
(m) $-(CH_2)_{0-3}C(=O)N(R^a)_2$, and
(n) $-(CH_2)_{0-3}C(=O)R^a$;

(4) a 5- or 6- or 7- membered saturated heterocyclic ring selected from piperidinyl, morpholinyl, thiomorpholinyl, thiazolidinyl, isothiazolidinyl, oxazolidinyl, isooxazolidinyl, pyrrolidinyl, imidazolidinyl, piperazinyl, tetrahydrofuranyl, pyrazolidinyl, hexahydropyrimidinyl, thiazinanyl, thiazepanyl, azepanyl, thiadiazepanyl, dithiazepanyl, diazepanyl; and wherein the heterocyclic ring is unsubstituted or substituted with 1 to 4 substituents independently selected from:

(a) halogen selected from -F, -Cl, and -Br,
(b) methyl or ethyl,
(c) $-CF_3$,
(d) methoxy,
(e) $-OCF_3$,
(f) -CN,
(g) =O,
(h) phenyl,
(i) benzyl,
(j) phenylethyl,
(k) -OH,
(l) $-(CH_2)_{0-3}C(=O)N(R^a)_2$,
(m) $-(CH_2)_{0-3}C(=O)R^a$,
(n) $N(R^a)-C(=O)R^a$,
(o) $N(R^a)-CO_2R^a$,
(p) $(CH_2)_{1-3}N(R^a)-C(=O)R^a$,
(q) $N(R^a)_2$,
(r) $(CH_2)_{1-3}N(R^a)_2$,
(s) SO_2R^a,
(t) $-(CH_2)_{0-3}C(=O)R^t$,
(u) $-R^t$,
(v) $-N(R^a)R^t$, and
(w) $-(CH_2)_{1-3}R^t$; and

(5) an 8- to 10- membered heterobicyclic ring selected from indolyl, benzotriazolyl, benzoimidazolyl, imidazo[4,5-b]pyridinyl, dihydroimidazo[4,5-b]pyridinyl, pyrazolo[4,3-c]pyridinyl, dihydropyrazolo[4,3-c]pyridinyl, tetrahydropyrazolo[4,3-c]pyridinyl, pyrrolo[1,2-a]pyrazinyl, dihydropyrrolo[1,2-a]pyrazinyl, tetrahydropyrrolo[1,2-a]pyrazinyl, octahydropyrrolo[1,2-a]pyrazinyl, isoindolyl, indazolyl, indolinyl, isoindolinyl, quinolinyl, isoquinolinyl, quinoxalinyl, quinazolinyl, cinnolinyl, chromanyl, isochromanyl, and 1,2,3,4-tetrahydro-1,8-naphthyridinyl, wherein the bicyclic ring is unsubstituted or substituted with 1 or 2 substituents independently selected from:

(a) halogen selected from -F, -Cl, and -Br,
(b) methyl or ethyl,

(c) $-CF_3$,
(d) methoxy,
(e) $-OCF_3$,
(f) -CN,
(g) =O, and
(h) -OH;

R^t is selected from pyrrolidinyl, pyrazolidinyl, imidazolinyl, piperidinyl, piperazinyl, pyrrolyl, pyridyl, imidazolyl, pyrazolyl, triazolyl, tetrazolyl, pyrazinyl, pyrimidinyl, and pyradizinyl; any one of which is unsubstituted or substituted with 1 or 2 substituents independently selected from -F, -Cl, -Br, oxo, methyl, and methoxy;

or a pharmaceutically acceptable salt thereof.

In an aspect of the seventeenth embodiment, the compound of Formula (IV) is as just defined above, except that:

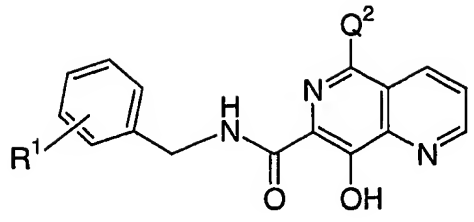
the definition of Q^2 does not include (56) $-N(R^a)SO_2R^k$;

parts (1)(b), (2(b), (3(b), (4(b), (5(b), and (6)(b) of the definition of R^k is methyl, instead of methyl or ethyl; and

in part (5) of the definition of R^k, the 5- or 6- or 7- membered saturated heterocyclic ring is selected from piperidinyl, morpholinyl, thiomorpholinyl, thiazolidinyl, isothiazolidinyl, oxazolidinyl, isooxazolidinyl, pyrrolidinyl, imidazolidinyl, piperazinyl, tetrahydrofuranyl, pyrazolidinyl, hexahydropyrimidinyl, thiazinanyl, thiazepanyl, and azepanyl.

In another aspect of the seventeenth embodiment, R^1 and R^2 in the compound of Formula (IV) are both chloro. In a feature of this aspect, the compound is a compound of Formula (VI) wherein Q^2 is as defined in the seventeenth embodiment.

A second class of the present invention is a compound of Formula (VII):

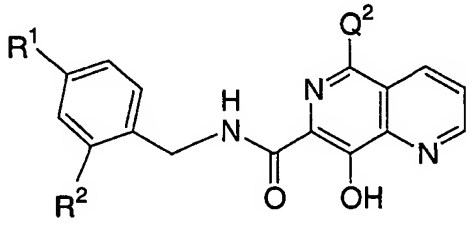


(VII);

wherein the variables are as defined in the seventeenth embodiment; or, alternatively, as originally defined, or as defined in any of the other preceding embodiments, classes, or sub-classes containing the variables;

or a pharmaceutically acceptable salt thereof.

A third sub-class of the present invention is compounds of Formula (V-A):



(V-A);

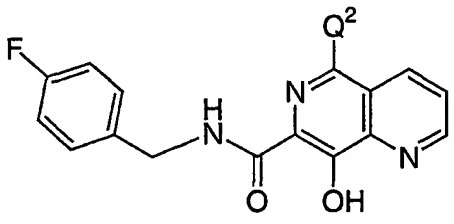
wherein each of the variables is as defined in the seventeenth embodiment, or, alternatively, as originally defined, or as defined in any of the other preceding embodiments, classes, or sub-classes containing the variables;

or a pharmaceutically acceptable salt thereof.

A fourth sub-class of the present invention is compounds of Formula (V-A), wherein R^1 is H or F, and R^2 is H or $-SO_2CH_3$, with the proviso that R^1 and R^2 are not both H; and Q^2 is as defined in the seventeenth embodiment, or as originally defined, or as defined in any of the other preceding embodiments, classes, or sub-classes containing Q^2;

or a pharmaceutically acceptable salt thereof.

A fifth sub-class of the present invention is a compound of Formula (VIII):



(VIII);

wherein Q^2 is as defined in the second class, or as originally defined or as defined in any of the other preceding embodiments, classes, or sub-classes containing Q^2;

or a pharmaceutically acceptable salt thereof.

In an aspect of each of the preceding classes and sub-classes,

Q^2 is:

(1) $-C(=O)N(R^a)_2$,
(2) $-CH_2C(=O)N(R^a)_2$,
(3) $-CH_2CH_2C(=O)N(R^a)_2$,
(4) $-S-CH_2-C(=O)N(R^a)_2$,
(5) $-O-CH_2-C(=O)N(R^a)_2$,
(6) $-N(R^a)-C(R^a)=O$,
(7) $-N(SO_2R^a)-CH_2-C(=O)N(R^a)_2$,
(8) $-N(R^a)-C(=O)-C(=O)-N(R^a)_2$,
(9) $-N(R^a)SO_2R^a$,
(10) $-CH=CH-C(=O)-N(R^a)_2$,
(11) $-N(R^a)CH_2-C(=O)N(R^a)_2$,
(12) $-N(R^a)-C(=O)-N(R^a)_2$,
(13) $-R^k$,
(14) $-(CH_2)_{1-3}R^k$, or
(15) $-N(R^c)-(CH_2)_{1-3}R^k$,

each R^a is independently -H or $-C_{1-4}$ alkyl;

each R^c is independently -H or $-C_{1-4}$ alkyl; and

R^k is a saturated heterocyclic ring selected from piperidinyl, morpholinyl, thiomorpholinyl, thiazolidinyl, isothiazolidinyl, oxazolidinyl, isooxazolidinyl, pyrrolidinyl, imidazolidinyl, piperazinyl, tetrahydrofuranyl, pyrazolidinyl, hexahydropyrimidinyl, 1,2-thiazinanyl, 1,4-thiazepanyl, 1,2,5-thiadiazepanyl, 1,5,2-dithiazepanyl, 1,4-diazepanyl, and 1,2,6-thiadiazinanyl, wherein the heterocyclic ring is unsubstituted or substituted with 1 to 4 substituents independently selected from:

(a) methyl or ethyl,
(b) =O,
(c) $-C(=O)N(R^a)_2$,
(d) $-CH_2C(=O)N(R^a)_2$,
(e) $-C(=O)R^a$, or
(f) $-SO_2R^a$;

or a pharmaceutically acceptable salt thereof.

In a feature of each these aspects, R^k is a saturated heterocyclic ring selected from piperidinyl, morpholinyl, thiomorpholinyl, thiazolidinyl, isothiazolidinyl, oxazolidinyl, isooxazolidinyl, pyrrolidinyl, imidazolidinyl, piperazinyl, tetrahydrofuranyl, pyrazolidinyl, hexahydropyrimidinyl, 1,2-thiazinanyl, 1,4-thiazepanyl, and 1,2,5-thiadiazepanyl, wherein the heterocyclic ring is unsubstituted or substituted with 1 to 4 substituents independently selected from:

(a) methyl,
(b) =O,
(c) $-C(=O)N(R^a)_2$, or
(d) $-CH_2C(=O)N(R^a)_2$.

In another aspect of each of the preceding classes and sub-classes, Q^2 is:

(1) $-C(=O)N(R^a)_2$,
(2) $-CH_2C(=O)N(R^a)_2$,
(3) $-CH_2CH_2C(=O)N(R^a)_2$,
(4) $-S-CH_2-C(=O)N(R^a)_2$,
(5) $-O-CH_2-C(=O)N(R^a)_2$,

(6) $-N(SO_2R^a)-CH_2-C(=O)N(R^a)_2$,
(7) $-N(R^a)-C(=O)-C(=O)-N(R^a)_2$,
(8) $-N(R^a)SO_2R^a$,
(9) $-CH=CH-C(=O)-N(R^a)_2$,
(10) $-N(R^a)CH_2-C(=O)N(R^a)_2$,
(11) $-N(R^a)-C(=O)-N(R^a)_2$,
(12) $-R^k$,
(13) $-(CH_2)_{1-2}R^k$, or
(14) $-NH-(CH_2)_{1-2}R^k$;

each R^a is independently methyl, ethyl, or isopropyl; and

R^k is a saturated heterocyclic ring selected from piperidinyl, morpholinyl, thiomorpholinyl, thiazolidinyl, isothiazolidinyl, oxazolidinyl, isooxazolidinyl, pyrrolidinyl, imidazolidinyl, piperazinyl, tetrahydrofuranyl, pyrazolidinyl, hexahydropyrimidinyl, 1,2-thiazinanyl, 1,4-thiazepanyl, 1,2,5-thiadiazepanyl, 1,5,2-dithiazepanyl, 1,4-diazepanyl, and 1,2,6-thiadiazinanyl, wherein the heterocyclic ring is unsubstituted or substituted with 1 to 4 substituents independently selected from:

(a) methyl or ethyl,
(b) =O,
(c) $-C(=O)NH_2$,
(d) $-C(=O)CH_3$, or
(e) $-SO_2CH_3$;

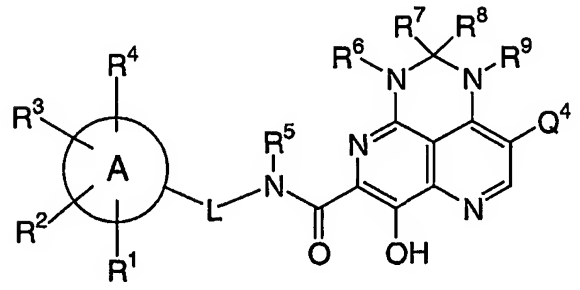
or a pharmaceutically acceptable salt thereof.

In a feature of each these aspects, R^k is a saturated heterocyclic ring selected from piperidinyl, morpholinyl, thiomorpholinyl, thiazolidinyl, isothiazolidinyl, oxazolidinyl, isooxazolidinyl, pyrrolidinyl, imidazolidinyl, piperazinyl, tetrahydrofuranyl, pyrazolidinyl, hexahydropyrimidinyl, 1,2-thiazinanyl, 1,4-thiazepanyl, and 1,2,5-thiadiazepanyl, wherein the heterocyclic ring is unsubstituted or substituted with 1 to 4 substituents independently selected from:

(a) methyl,
(b) =O, or

(c) $-C(=O)NH_2$.

An eighteenth embodiment of the present invention is a compound of Formula (IX):



(IX);

wherein

each of R^6 and R^9 is independently:

(1) -H
(2) $-C_{1-4}$ alkyl,
(3) $-C_{1-4}$ fluoroalkyl,
(4) $-C_{1-4}$ alkyl-OR^a,
(5) $-C_{1-4}$ alkyl-$S(O)_nR^a$,
(6) $-C_{1-4}$ alkyl-$N(R^a)_2$,
(7) $-C_{1-4}$ alkyl-$C(=O)$-$N(R^a)_2$,
(8) $-C_{1-4}$ alkyl-CO_2R^a, and
(9) $-C_{1-4}$ alkyl substituted with R^k; and

each of R^7 and R^8 is independently:

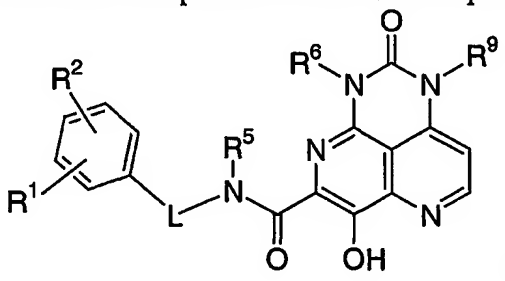
(1) -H
(2) $-C_{1-4}$ alkyl,
(3) $-C_{1-4}$ fluoroalkyl,
(4) $-C_{1-4}$ alkyl-OR^a,
(5) $-C_{1-4}$ alkyl-SR^a,
(6) $-C_{1-4}$ alkyl-$N(R^a)_2$,
(7) $-C_{1-4}$ alkyl-$C(=O)$-$N(R^a)_2$,
(8) $-C_{1-4}$ alkyl-CO_2R^a, and
(9) $-C_{1-4}$ alkyl substituted with R^k;

or R^7 and R^8 together form oxo;

and all other variables are as originally defined or as defined in any of the preceding embodiments;

or a pharmaceutically acceptable salt thereof.

A third class of the present invention is compounds of Formula (X):

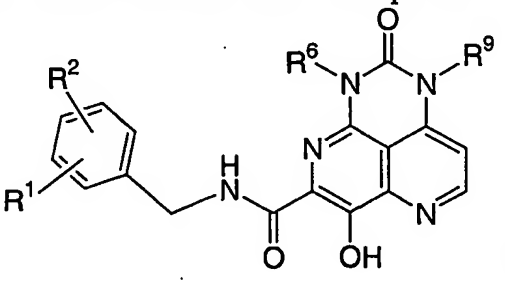


(X);

wherein each of the variables is as defined in the eighteenth embodiment;

or a pharmaceutically acceptable salt thereof.

A sub-class of the third class is a compound of Formula (XI):

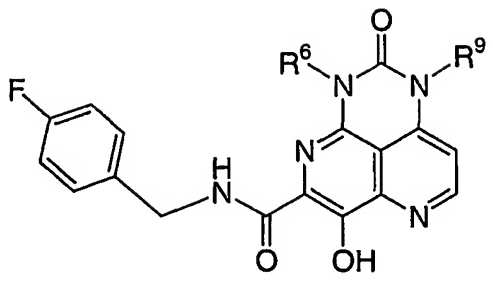


(XI);

wherein each of the variables is as defined in the third class;

or a pharmaceutically acceptable salt thereof.

Another sub-class of the third class is a compound of Formula (XII):


(XII);

wherein each of the variables is as defined in the third class;

or a pharmaceutically acceptable salt thereof.

An aspect of the sub-class is a compound of Formula (XII), wherein

R^6 is:

(1) -H
(2) methyl,
(3) ethyl
(4) $-CF_3$,
(4) $-(CH_2)_{1-3}-OR^a$,
(5) $-(CH_2)_{1-3}-SR^a$,
(6) $-(CH_2)_{1-3}-SO_2R^a$,
(7) $-(CH_2)_{1-3}-N(R^a)_2$,
(8) $-(CH_2)_{1-3}-C(=O)-N(R^a)_2$, or
(9) $-(CH_2)_{1-3}-CO_2R^a$;

R^9 is:

(1) -H
(2) methyl,
(3) ethyl,
(4) $-CF_3$,
(4) $-(CH_2)_{1-3}-OR^a$,
(5) $-(CH_2)_{1-3}-SR^a$,
(6) $-(CH_2)_{1-3}-SO_2R^a$,
(7) $-(CH_2)_{1-3}-N(R^a)_2$,

(8) $-(CH_2)_{1-3}-C(=O)-N(R^a)_2$,
(9) $-(CH_2)_{1-3}-CO_2R^a$, or
(10) $-(CH_2)_{1-3}-R^k$;

each R^a is independently -H, methyl, or ethyl;

R^k is a saturated heterocyclic ring selected from piperidinyl, morpholinyl, thiomorpholinyl, thiazolidinyl, isothiazolidinyl, oxazolidinyl, isooxazolidinyl, pyrrolidinyl, imidazolidinyl, piperazinyl, tetrahydrofuranyl, and pyrazolidinyl; and wherein the heterocyclic ring is unsubstituted or substituted with from 1 to 3 substituents independently selected from:

(a) halogen selected from -F, -Cl, and -Br,
(b) methyl,
(c) $-CF_3$,
(d) methoxy,
(e) $-OCF_3$,
(f) -CN, and
(g) =O;

or a pharmaceutically acceptable salt thereof.

Exemplary compounds of the invention include compounds selected from the group consisting of

N-(3,5-dichlorobenzyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide;

N-(2,5-dichlorobenzyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide;

N-[(1R,S)-2,3-dihydro-1H-inden-1-yl]-8-hydroxy-1,6-naphthyridine-7-carboxamide;

N-[2-(3-chlorophenyl)ethyl]-8-hydroxy-1,6-naphthyridine-7-carboxamide;

N-[2-(2-chlorophenyl)ethyl]-8-hydroxy-1,6-naphthyridine-7-carboxamide;

N-[2-(1,1'-biphenyl-4-yl)ethyl]-8-hydroxy-1,6-naphthyridine-7-carboxamide;

8-hydroxy-N-[2-(4-phenoxyphenyl)ethyl]-1,6-naphthyridine-7-carboxamide;

8-hydroxy-N-(3-phenylpropyl)-1,6-naphthyridine-7-carboxamide;

N-(1,1'-biphenyl-2-ylmethyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide;

N-(1,1'-biphenyl-3-ylmethyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide;

8-hydroxy-N-phenyl-1,6-naphthyridine-7-carboxamide;

8 N-(2-chlorobenzyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide;

N-benzyl-8-hydroxy-N-methyl-1,6-naphthyridine-7-carboxamide;

8-hydroxy-N-(1-methyl-1-phenylethyl)-1,6-naphthyridine-7-carboxamide;

8-hydroxy-N-(2-phenylethyl)-1,6-naphthyridine-7-carboxamide;

8-hydroxy-N-(1-naphthylmethyl)-1,6-naphthyridine-7-carboxamide;

N-benzyl-8-hydroxy-N-phenyl-1,6-naphthyridine-7-carboxamide;

N-(3-chlorobenzyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide;

N-(4-chlorobenzyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide;

Methyl (2S)-{[(8-hydroxy-1,6-naphthyridin-7-yl)carbonyl]amino} (phenyl)ethanoate;

Ethyl N-benzyl-N-[(8-hydroxy-1,6-naphthyridin-7-yl)carbonyl]glycinate;

N-benzyl-8-hydroxy-N-(2-phenylethyl)-1,6-naphthyridine-7-carboxamide;

N-(1,2-diphenylethyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide;

N-(2,3-dihydro-1H-inden-2-yl)-8-hydroxy-1,6-naphthyridine-7-carboxamide;

N-benzyl-8-hydroxy-1,6-naphthyridine-7-carboxamide;

N-(2-anilinoethyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide;

N-(2,2-diphenylethyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide;

N-(3,3-diphenylpropyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide;

N-(2-chloro-6-phenoxybenzyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide;

Methyl (2R)-{[(8-hydroxy-1,6-naphthyridin-7-yl)carbonyl]amino} (phenyl)ethanoate;

8-hydroxy-N-(1,2,3,4-tetrahydronaphthalen-1-yl)-1,6-naphthyridine-7-carboxamide;

N-(2,3-dihydro-1H-inden-1-ylmethyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide;

8-hydroxy-N-(6,7,8,9-tetrahydro-5H-benzo[a][7]annulen-6-ylmethyl)-1,6-naphthyridine-7-carboxamide;

8-hydroxy-N-[2-(1-naphthylamino)ethyl]-1,6-naphthyridine-7-carboxamide;

N-(2,3-dihydro-1H-inden-2-ylmethyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide;

8-hydroxy-N-[(1R)-1-phenylethyl]-1,6-naphthyridine-7-carboxamide;

8-hydroxy-N-[(1S)-1-phenylethyl]-1,6-naphthyridine-7-carboxamide;

8-hydroxy-N-(3-hydroxy-1-phenylpropyl)-1,6-naphthyridine-7-carboxamide;

N-[2-(4-chlorophenyl)ethyl]-8-hydroxy-1,6-naphthyridine-7-carboxamide;

8-hydroxy-N-[(1R)-2-hydroxy-1-phenylethyl]-1,6-naphthyridine-7-carboxamide;

N-[(1S)-1-benzyl-2-hydroxyethyl]-8-hydroxy-1,6-naphthyridine-7-carboxamide;

N-[(1R)-1-benzyl-2-hydroxyethyl]-8-hydroxy-1,6-naphthyridine-7-carboxamide;

8-hydroxy-N-(2-hydroxy-2-phenylethyl)-1,6-naphthyridine-7-carboxamide;

5-chloro-N-(3,5-dichlorobenzyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide;

N-(3,5-dichlorobenzyl)-8-hydroxy-5-piperidin-1-yl-1,6-naphthyridine-7-carboxamide;

N-(3,5-dichlorobenzyl)-8-hydroxy-5-phenyl-1,6-naphthyridine-7-carboxamide;

N-(3,5-dichlorobenzyl)-8-hydroxy-5-(1H-imidazol-1-yl)-1,6-naphthyridine-7-carboxamide;

N-(3,5-dichlorobenzyl)-8-hydroxy-5-morpholin-4-yl-1,6-naphthyridine-7-carboxamide;

(±)-8-hydroxy-N-[(*cis*)-3-phenyl-2,3-dihydro-1H-inden-1-yl]-1,6-naphthyridine-7-carboxamide

5-bromo-N-(3,5-dichlorobenzyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide;

N-(benzyl)-8-hydroxy-5-phenyl-1,6-naphthyridine-7-carboxamide;

N-(2,3-dihydro-1H-inden-1-yl)-8-hydroxy-5-phenyl-1,6-naphthyridine-7-carboxamide;

8-hydroxy-N-(1-naphthylmethyl)-5-phenyl-1,6-naphthyridine-7-carboxamide;

N-(2,5-dichlorobenzyl)-8-hydroxy-5-phenyl-1,6-naphthyridine-7-carboxamide;

N-(3-chlorobenzyl)-8-hydroxy-5-phenyl-1,6-naphthyridine-7-carboxamide;

N-[(1S)-2,3-dihydro-1H-inden-1-yl]-8-hydroxy-1,6-naphthyridine-7-carboxamide;

N-(3,5-dichlorobenzyl)-8-hydroxy-5-phenoxy-1,6-naphthyridine-7-carboxamide;

N-(3,5-dichlorobenzyl)-8-hydroxy-5-(4-methylpiperazin-1-yl)-1,6-naphthyridine-7-carboxamide;

5-(4-benzylpiperazin-1-yl)-N-(3,5-dichlorobenzyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide;

N-(3,5-dichlorobenzyl)-5-{4-[2-(formylamino)ethyl]piperazin-1-yl}-8-hydroxy-1,6-naphthyridine-7-carboxamide;

N-(3,5-dichlorobenzyl)-8-hydroxy-5-(4-pyridin-2-ylpiperazin-1-yl)-1,6-naphthyridine-7-carboxamide;

N-(3,5-dichlorobenzyl)-8-hydroxy-5-(4-pyrrolidin-1-ylpiperidin-1-yl)-1,6-naphthyridine-7-carboxamide;

5-anilino-N-(3,5-dichlorobenzyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide;

N-(3,5-dichlorobenzyl)-5-{[3-(formylamino)propyl]amino}-8-hydroxy-1,6-naphthyridine-7-carboxamide;

N-(3,5-dichlorobenzyl)-5-{[2-(dimethylamino)ethyl]amino}-8-hydroxy-1,6-naphthyridine-7-carboxamide;

N-(3,5-dichlorobenzyl)-8-hydroxy-5-[(2-morpholin-4-ylethyl)amino]-1,6-naphthyridine-7-carboxamide;

5-[(1-benzylpiperidin-4-yl)amino]-N-(3,5-dichlorobenzyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide;

N-(3,5-dichlorobenzyl)-5-[[2-(dimethylamino)ethyl](methyl)amino]-8-hydroxy-1,6-naphthyridine-7-carboxamide;

8-Hydroxy-5-phenylsulfanyl-[1,6]naphthyridine-7-carboxylic acid 3,5-dichlorobenzylamide;

5-benzenesulfonyl-8-hydroxy-[1,6]naphthyridine-7-carboxylic acid 3,5-dichlorobenzylamide;

tert-butyl 1-(7-{[(3,5-dichlorobenzyl)amino]carbonyl}-8-hydroxy-1,6-naphthyridin-5-yl)pyrrolidin-3-ylcarbamate;

5-(3-aminopyrrolidin-1-yl)-N-(3,5-dichlorobenzyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide trifluoroacetate;

N-(3,5-dichlorobenzyl)-8-hydroxy-5-(4*H*-1,2,4-triazol-4-yl)-1,6-naphthyridine-7-carboxamide;

N-(3,5-dichlorobenzyl)-8-hydroxy-5-(1*H*-1,2,4-triazol-1-yl)-1,6-naphthyridine-7-carboxamide;

N-(3,5-dichlorobenzyl)-8-hydroxy-5-(3-hydroxypyrrolidin-1-yl)-1,6-naphthyridine-7-carboxamide;

5-[3-(acetylamino)pyrrolidin-1-yl]-*N*-(3,5-dichlorobenzyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide;

N-(3,5-dichlorobenzyl)-5-(4-formylpiperazin-1-yl)-8-hydroxy-1,6-naphthyridine-7-carboxamide;

1-(7-{[(3,5-dichlorobenzyl)amino]carbonyl}-8-hydroxy-1,6-naphthyridin-5-yl)piperazine;

8-Hydroxy-5-(3-hydroxy-prop-1-ynyl)-[1,6]naphthyridine-7-carboxylic acid 3,5-dichloro-benzylamide;

1-(7-{[(3,5-dichlorobenzyl)amino]carbonyl}-8-hydroxy-1,6-naphthyridin-5-yl)-4-(2-oxo-2-pyrrolidin-1-ylethyl)piperazine;

8-Hydroxy-5-(3-piperidin-1-yl-prop-1-ynyl)-[1,6]naphthyridine-7-carboxylic acid 3,5-dichloro-benzylamide;

N-(3,5-dichlorobenzyl)-8-hydroxy-5-thiomorpholin-4-yl-1,6-naphthyridine-7-carboxamide;

5-[3-(aminocarbonyl)piperidin-1-yl]-*N*-(3,5-dichlorobenzyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide;

1-(7-{[(3,5-dichlorobenzyl)amino]carbonyl}-8-hydroxy-1,6-naphthyridin-5-yl)-4-(2-phenylethyl)piperazine;

4-[(7-{[(3,5-dichlorobenzyl)amino]carbonyl}-8-hydroxy-1,6-naphthyridin-5-yl)amino]pyridine;

5-[(cyclopropylmethyl)amino]-*N*-(3,5-dichlorobenzyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide;

N-(3,5-dichlorobenzyl)-5-{[2-(formylamino)ethyl]amino}-8-hydroxy-1,6-naphthyridine-7-carboxamide;

2-[(7-{[(3,5-dichlorobenzyl)amino]carbonyl}-8-hydroxy-1,6-naphthyridin-5-yl)amino]ethanamine;

N-(3,5-dichlorobenzyl)-8-hydroxy-5-[(2-methoxyethyl)amino]-1,6-naphthyridine-7-carboxamide;

N-(3,5-dichlorobenzyl)-8-hydroxy-5-{[2-(methylthio)ethyl]amino}-1,6-naphthyridine-7-carboxamide;

1-{2-[(7-{[(3,5-dichlorobenzyl)amino]carbonyl}-8-hydroxy-1,6-naphthyridin-5-yl)amino]ethyl}pyrrolidine;

1 *N*-(3,5-dichlorobenzyl)-8-hydroxy-5-pyrrolidin-1-yl-1,6-naphthyridine-7-carboxamide;

3-{2-[(7-{[(3,5-dichlorobenzyl)amino]carbonyl}-8-hydroxy-1,6-naphthyridin-5-yl)amino]ethyl}pyridine;

1-{3-[(7-{[(3,5-dichlorobenzyl)amino]carbonyl}-8-hydroxy-1,6-naphthyridin-5-yl)amino]propyl}-1*H*-imidazoline;

1-{3-[(7-{[(3,5-dichlorobenzyl)amino]carbonyl}-8-hydroxy-1,6-naphthyridin-5-yl)amino]propyl}pyrrolidine;

1-(2-aminoethyl)-4-(7-{[(3,5-dichlorobenzyl)amino]carbonyl}-8-hydroxy-1,6-naphthyridin-5-yl)piperazine;

N-(3,5-dichlorobenzyl)-8-hydroxy-5-[(2-phenoxyethyl)amino]-1,6-naphthyridine-7-carboxamide;

N-(3,5-dichlorobenzyl)-8-hydroxy-5-{[3-(2-oxopyrrolidin-1-yl)propyl]amino}-1,6-naphthyridine-7-carboxamide;

2-[benzyl(7-{[(3,5-dichlorobenzyl)amino]carbonyl}-8-hydroxy-1,6-naphthyridin-5-yl)amino]ethanamine;

1-{3-[(7-{[(3,5-dichlorobenzyl)amino]carbonyl}-8-hydroxy-1,6-naphthyridin-5-yl)amino]propyl}-4-methylpiperazine;

1:1 mixture of 1-(7-{[(3,5-dichlorobenzyl)amino]carbonyl}-8-hydroxy-1,6-naphthyridin-5-yl)-1*H*-imidazo[4,5-*b*]pyridine and 3-(7-{[(3,5-dichlorobenzyl)amino]carbonyl}-8-hydroxy-1,6-naphthyridin-5-yl)-3*H*-imidazo[4,5-*b*]pyridine;

N-(3,5-dichlorobenzyl)-8-hydroxy-5-{[4-(3-methyl-2-oxoimidazolidin-1-yl)phenyl]amino}-1,6-naphthyridine-7-carboxamide;

N-(3,5-dichlorobenzyl)-8-hydroxy-5-(1,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridin-5-yl)-1,6-naphthyridine-7-carboxamide;

N-(3,5-dichlorobenzyl)-8-hydroxy-5-({[(2*R*)-5-oxopyrrolidin-2-yl]methyl}amino)-1,6-naphthyridine-7-carboxamide;

N-(3,5-dichlorobenzyl)-8-hydroxy-5-{[(5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)methyl]amino}-1,6-naphthyridine-7-carboxamide;

2-(7-{[(3,5-dichlorobenzyl)amino]carbonyl}-8-hydroxy-1,6-naphthyridin-5-yl)octahydropyrrolo[1,2-*a*]pyrazine;

N-(3,5-dichlorobenzyl)-8-hydroxy-5-[4-(pyrimidin-2-ylamino)piperidin-1-yl]-1,6-naphthyridine-7-carboxamide

2-{2-[(7-{[(3,5-dichlorobenzyl)amino]carbonyl}-8-hydroxy-1,6-naphthyridin-5-yl)(methyl)amino]ethyl}pyridine;

N-(3,5-dichlorobenzyl)-5-(dimethylamino)-8-hydroxy-1,6-naphthyridine-7-carboxamide;

8-Hydroxy-5-(3-morpholin-4-yl-prop-1-ynyl)-[1,6]naphthyridine-7-carboxylic acid 3,5-dichloro-benzylamide;

N-(3,5-difluorobenzyl)-8-hydroxy-5-(methylsulfonyl)-1,6-naphthyridine-7-carboxamide;

5-cyano-N-(2,3-dimethoxybenzyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide;

N-(3,5-dichlorobenzyl)-8-hydroxy-5-thien-2-yl-1,6-naphthyridine-7-carboxamide;

8-hydroxy-5-phenylsulfanyl-[1,6]naphthyridine-7-carboxylic acid 2-methylsulfanylbenzylamide;

N-(2,3-dimethoxybenzyl)-8-hydroxy-5-(methylsulfonyl)-1,6-naphthyridine-7-carboxamide;

N-(3,5-dichlorobenzyl)-8-hydroxy-5-[(2-hydroxyethyl)amino]-1,6-naphthyridine-7-carboxamide;

N-(3,5-dichlorobenzyl)-8-hydroxy-5-(propylamino)-1,6-naphthyridine-7-carboxamide;

N-(3,5-dichlorobenzyl)-8-hydroxy-5-[(1H-imidazol-4-ylethyl)amino]-1,6-naphthyridine-7-carboxamide;

N-(3,5-dichlorobenzyl)-8-hydroxy-5-[(3-phenylprop-1-yl)amino]-1,6-naphthyridine-7-carboxamide;

N-(3,5-dichlorobenzyl)-8-hydroxy-5-[(3-morpholin-4-ylpropyl)amino]-1,6-naphthyridine-7-carboxamide;

N-(3,5-dichlorobenzyl)-8-hydroxy-5-[4-(pyridin-2-ylmethyl)piperazin-1-yl]-1,6-naphthyridine-7-carboxamide;

N-(3,5-dichlorobenzyl)-8-hydroxy-5-[(2-morpholin-4-yl-2-pyridin-3-ylethyl)amino]-1,6-naphthyridine-7-carboxamide;

N-(2,3-dimethoxybenzyl)-5-{[4-(dimethylamino)phenyl]thio}-8-hydroxy-1,6-naphthyridine-7-carboxamide;

8-hydroxy-6-methyl-[1,6]naphthyridine-7-carboxylic acid 3,5-dichloro-benzylamide;

8-hydroxy-6-methyl-[1,6]naphthyridine-7-carboxylic acid 4-fluoro-benzylamide;

5-bromo-N-(4-fluorobenzyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide;

1-(7-{[(4-fluorobenzyl)amino]carbonyl}-8-hydroxy-1,6-naphthyridin-5-yl)-4-methylpiperazine;

1-(7-{[(4-fluorobenzyl)amino]carbonyl}-8-hydroxy-1,6-naphthyridin-5-yl)piperazine;

5-[[2-(dimethylamino)-2-oxoethyl](methyl)amino]-N-(4-fluorobenzyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide;

N-1-(7-{[(4-fluorobenzyl)amino]carbonyl}-8-hydroxy-1,6-naphthyridin-5-yl)-N-1-,N-2-,N-2-trimethylethanediamide ;

N-(4-fluorobenzyl)-5-(2,6-dioxohexahydropyrimidin-4-yl)-8-hydroxy-[1,6]napthyridine-7-carboxamide;

5-(1,3-dimethyl-2,6-dioxohexahydro-4-pyrimidinyl)-N-(4-fluorobenzyl)-8-hydroxy[1,6]-naphthyridine-7-carboxamide;

5-(1-methyl-2,6-dioxohexahydro-4-pyrimidinyl)-N-(4-fluorobenzyl)-8-hydroxy[1,6]-naphthyridine-7-carboxamide;

5-(3-methyl-2,6-dioxohexahydro-4-pyrimidinyl)-N-(4-fluorobenzyl)-8-hydroxy[1,6]-naphthyridine-7-carboxamide;

N-(4-fluorobenzyl)-8-hydroxy-5-(5-oxo-1,4-thiazepan-7-yl)[1,6]naphthyridine-7-carboxamide;

N-(4-fluorobenzyl)-8-hydroxy-5-(1-oxido-5-oxo-1,4-thiazepan-7-yl)-[1,6]naphthyridine-7-carboxamide;

N-(4-fluorobenzyl)-8-hydroxy-5-(1,1-dioxido-5-oxo-1,4-thiazepan-7-yl)[1,6]-naphthyridine-7-carboxamide;

N-(4-fluorobenzyl)-5-{[2-(dimethylamino)-2-oxoethyl]sulfanyl}-8-hydroxy-[1,6]napthyridine-7-carboxamide;

N-(4-fluorobenzyl)-5-[2-(dimethylamino)-2-oxoethoxy]-8-hydroxy-[1,6]napthyridine-7-carboxamide;

N-(4-fluorobenzyl)-5-{[2-(dimethylamino)-2-oxoethyl](methylsulfonyl)amino}-8-hydroxy-[1,6]napthyridine-7-carboxamide;

N-(4-fluorobenzyl)-5-[3-(dimethylamino)-3-oxopropyl]-8-hydroxy-[1,6]napthyridine-7-carboxamide;

N-(4-fluorobenzyl)-5-[(1*E*)-3-(dimethylamino)-3-oxo-1-propenyl]-8-hydroxy-[1,6]napthyridine-7-carboxamide;

N-(4-fluorobenzyl)-5-[2-(3-oxo-1-piperazinyl)ethyl]-8-hydroxy-[1,6]napthyridine-7-carboxamide;

N-(4-fluorobenzyl)-5-[2-(2-oxo-1-imidazolidinyl)ethyl]-8-hydroxy-[1,6]napthyridine-7-carboxamide;

N-(4-fluorobenzyl)-5-[2-(2-oxo-1-piperazinyl)ethyl]-8-hydroxy-[1,6]napthyridine-7-carboxamide;

5-(1,1-dioxido-1,2-thiazinan-2-yl)-*N*-(4-fluorobenzyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide;

5-(1,1-dioxidoisothiazolidin-2-yl)-*N*-(4-fluorobenzyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide;

N-(4-fluorobenzyl)-8-hydroxy-5-[methyl(methylsulfonyl)amino]-1,6-naphthyridine-7-carboxamide;

5-[acetyl(methyl)amino]-*N*-(4-fluorobenzyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide;

5-[[(dimethylamino)carbonyl](methyl)amino]-*N*-(4-fluorobenzyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide;

N-(4-fluorobenzyl)-6-hydroxy-3-methyl-1-(2-morpholin-4-ylethyl)-2-oxo-2,3-dihydro-1H-pyrimido[4,5,6-de]-1,6-naphthyridine-5-carboxamide;

N-(4-fluorobenzyl)-8-hydroxy-5-thiomorpholin-4-yl-1,6-naphthyridine-7-carboxamide;

5-(1,1-dioxidothiomorpholin-4-yl)-*N*-(4-fluorobenzyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide;

N-(4-fluorobenzyl)-8-hydroxy-5-(4-methyl-3-oxopiperazin-1-yl)-1,6-naphthyridine-7-carboxamide;

1-(7-{[4-fluorobenzyl)amino]carbonyl}-8-hydroxy-1,6-naphthyridin-5-yl-L-prolinamide;

N-(4-fluorobenzyl)-8-hydroxy-5-(2-oxotetrahydropyrimidin-1(2*H*)-yl)-1,6-naphthyridine-7-carboxamide;

N-(4-fluorobenzyl)-8-hydroxy-5-(2-oxoimidazolidin-1-yl)-1,6-naphthyridine-7-carboxamide;

N-7-(4-fluorobenzyl)-8-hydroxy-*N* 5, *N* 5-dimethyl-1,6-naphthyridine-5,7-dicarboxamide;

N 7-(4-fluorobenzyl)-8-hydroxy-*N* 5-isopropyl-*N* 5-methyl-1,6-naphthyridine-5,7-dicarboxamide;

N 7-(4-fluorobenzyl)-8-hydroxy-*N* 5-(2-morpholin-4-ylethyl)-1,6-naphthyridine-5,7-dicarboxamide;

N 5-[2-(dimethylamino)-2-oxoethyl]-*N* 7-(4-fluorobenzyl)-8-hydroxy-*N* 5-methyl-1,6-naphthyridine-5,7-dicarboxamide;

N-(4-fluorobenzyl)-5-(1,1-dioxido-4-oxo-1,2,5-thiadiazepan-2-yl)-8-hydroxy-[1,6]napthyridine-7-carboxamide;

N-(4-fluorobenzyl)-5-(1,1-dioxido-5-methyl-4-oxo-1,2,5-thiadiazepan-2-yl)-8-hydroxy-[1,6]napthyridine-7-carboxamide;

N-(4-fluorobenzyl)-5-(1,1-dioxido-5-ethyl-4-oxo-1,2,5-thiadiazepan-2-yl)-8-hydroxy-[1,6]napthyridine-7-carboxamide;

N-(4-fluorobenzyl)-5-(1,1-dioxido-1,5,2-dithiazepan-2-yl)-8-hydroxy-[1,6]napthyridine-7-carboxamide;

N-(4-fluorobenzyl)-5-(1,1,5,5-tetraoxido-1,5,2-dithiazepan-2-yl)-8-hydroxy-[1,6]napthyridine-7-carboxamide;

N-(4-fluorobenzyl)-5-(1,4-dimethyl-7-oxo-1,4-diazepan-5-yl)-8-hydroxy-[1,6]-napthyridine-7-carboxamide;

N-(4-fluorobenzyl)-5-(1-methyl-7-oxo-1,4-diazepan-5-yl)-8-hydroxy-[1,6]-napthyridine-7-carboxamide;

N-(4-Fluorobenzyl)-5-(7-oxo-1,4-diazepan-5-yl)-8-hydroxy-[1,6]-napthyridine-7-carboxamide

N-(4-fluorobenzyl)-5-[4-(methylsulfonyl)thiomorpholin-2-yl]-8-hydroxy-[1,6]napthyridine-7-carboxamide;

N-(4-fluorobenzyl)-5-[4-(methylsulfonyl)-1-oxidothiomorpholin-2-yl]-8-hydroxy-[1,6]napthyridine-7-carboxamide;

N-(4-fluorobenzyl)-5-[4-(methylsulfonyl)-1,1-dioxidothiomorpholin-2-yl]-8-hydroxy-[1,6]napthyridine-7-carboxamide;

N-(4-fluorobenzyl)-5-(2-Acetyl-1-methylpyrazolidin-3-yl)-8-hydroxy-[1,6]napthyridine-7-carboxamide;

N-(4-fluorobenzyl)-5-(1,1-dioxido-1,2,5-thiadiazepan-2-yl)-8-hydroxy-[1,6]napthyridine-7-carboxamide;

N-(4-fluorobenzyl)-8-hydroxy-5-[5-(methylsulfonyl)-1,1-dioxido-1,2,5-thiadiazepan-2-yl]-1,6-naphthyridine-7-carboxamide;

N-(4-fluorobenzyl)-8-hydroxy-5(6-methyl-1,1-dioxido-1,2,6-thiadiazinan-2yl)-1,6-naphthyridine-7-carboxamide;

N-(4-fluorobenzyl)-8-hydroxy-5-{methyl[(1-methyl-1*H*-imidazol-4-yl)sulfonyl]amino}-1,6-naphthyridine-7-carboxamide;

N-[4-fluoro-2-(methylsulfonyl)benzyl]-8-hydroxy-5-{methyl[(1-methyl-1*H*-imidazol-4-yl)sulfonyl]amino}-1,6-naphthyridine-7-carboxamide;

N-7-[4-fluoro-2-(methylsulfonyl)benzyl]-8-hydroxy-N-5-,N-5-dimethyl-1,6-naphthyridine-5,7-dicarboxamide;

N-[4-fluoro-2-(methylsulfonyl)benzyl]-8-hydroxy-5-(1,1-dioxido-1,2-thiazinan-2-yl)-1,6-naphthyridine-7-carboxamide

N-(2-(methylsulfonyl)benzyl)-5-(1,1-dioxido-1,2-thiazinan-2-yl)-8-hydroxy-1,6-naphthyridine-7-carboxamide;

N-(2-[(dimethylaminosulfonyl]-4-fluorobenzyl)-5-(1,1-dioxido-1,2-thiazinan-2-yl)-8-hydroxy-1,6-naphthyridine-7-carboxamide;

N-(4-fluorobenzyl)-8-hydroxy-5-(1-methyl-5-oxopyrrolidin-3-yl)-1,6-naphthyridine-7-carboxamide;

and pharmaceutically acceptable salts thereof.

In one aspect, the present invention is a compound selected from the group consisting of

1-(7-{[(4-fluorobenzyl)amino]carbonyl}-8-hydroxy-1,6-naphthyridin-5-yl)-4-methylpiperazine;

1-(7-{[(4-fluorobenzyl)amino]carbonyl}-8-hydroxy-1,6-naphthyridin-5-yl)piperazine;

N-(3,5-dichlorobenzyl)-5-(4-formylpiperazin-1-yl)-8-hydroxy-1,6-naphthyridine-7-carboxamide;

N-(3,5-dichlorobenzyl)-5-{4-[2-(formylamino)ethyl]piperazin-1-yl}-8-hydroxy-1,6-naphthyridine-7-carboxamide;

N-(3,5-dichlorobenzyl)-8-hydroxy-5-[4-(pyridin-2-ylmethyl)piperazin-1-yl]-1,6-naphthyridine-7-carboxamide;

1-(7-{[(3,5-dichlorobenzyl)amino]carbonyl}-8-hydroxy-1,6-naphthyridin-5-yl)-4-(2-oxo-2-pyrrolidin-1-ylethyl)piperazine;

1-(7-{[(3,5-dichlorobenzyl)amino]carbonyl}-8-hydroxy-1,6-naphthyridin-5-yl)piperazine;

2-(7-{[(3,5-dichlorobenzyl)amino]carbonyl}-8-hydroxy-1,6-naphthyridin-5-yl)octahydropyrrolo[1,2-*a*]pyrazine;

N-(3,5-dichlorobenzyl)-8-hydroxy-5-(1,4,6,7-tetrahydro-5*H*-pyrazolo[4,3-*c*]pyridin-5-yl)-1,6-naphthyridine-7-carboxamide;

N-(3,5-dichlorobenzyl)-8-hydroxy-5-{[4-(3-methyl-2-oxoimidazolidin-1-yl)phenyl]amino}-1,6-naphthyridine-7-carboxamide;

5-[3-(aminocarbonyl)piperidin-1-yl]-*N*-(3,5-dichlorobenzyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide;

N-(3,5-dichlorobenzyl)-8-hydroxy-5-(4-pyrrolidin-1-ylpiperidin-1-yl)-1,6-naphthyridine-7-carboxamide;

N-(3,5-dichlorobenzyl)-8-hydroxy-5-[(2-morpholin-4-ylethyl)amino]-1,6-naphthyridine-7-carboxamide;

N-(3,5-dichlorobenzyl)-8-hydroxy-5-(4-methylpiperazin-1-yl)-1,6-naphthyridine-7-carboxamide;

8-hydroxy-6-methyl-[1,6]naphthyridine-7-carboxylic acid 3,5-dichloro-benzylamide;

N-(3,5-dichlorobenzyl)-8-hydroxy-5-[4-(pyrimidin-2-ylamino)piperidin-1-yl]-1,6-naphthyridine-7-carboxamide

N-(3,5-dichlorobenzyl)-8-hydroxy-5-[(3-morpholin-4-ylpropyl)amino]-1,6-naphthyridine-7-carboxamide;

N-(3,5-dichlorobenzyl)-8-hydroxy-5-[(2-morpholin-4-yl-2-pyridin-3-ylethyl)amino]-1,6-naphthyridine-7-carboxamide;

2-{2-[(7-{[(3,5-dichlorobenzyl)amino]carbonyl}-8-hydroxy-1,6-naphthyridin-5-yl)(methyl)amino]ethyl}pyridine;

N-(3,5-dichlorobenzyl)-8-hydroxy-5-(4-pyridin-2-ylpiperazin-1-yl)-1,6-naphthyridine-7-carboxamide;

and pharmaceutically acceptable salts thereof.

In another aspect, the present invention is a compound selected from the group consisting of

5-[[2-(dimethylamino)-2-oxoethyl](methyl)amino]-N-(4-fluorobenzyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide;

N-1-(7-{[(4-fluorobenzyl)amino]carbonyl}-8-hydroxy-1,6-naphthyridin-5-yl)-N-1-,N-2-,N-2-trimethylethanediamide ;

N-(4-fluorobenzyl)-5-(2,6-dioxohexahydropyrimidin-4-yl)-8-hydroxy-[1,6]napthyridine-7-carboxamide;

5-(1,3-dimethyl-2,6-dioxohexahydro-4-pyrimidinyl)-N-(4-fluorobenzyl)-8-hydroxy[1,6]-naphthyridine-7-carboxamide;

5-(1-methyl-2,6-dioxohexahydro-4-pyrimidinyl)-N-(4-fluorobenzyl)-8-hydroxy[1,6]-naphthyridine-7-carboxamide;

5-(3-methyl-2,6-dioxohexahydro-4-pyrimidinyl)-N-(4-fluorobenzyl)-8-hydroxy[1,6]-naphthyridine-7-carboxamide;

N-(4-fluorobenzyl)-8-hydroxy-5-(5-oxo-1,4-thiazepan-7-yl)[1,6]naphthyridine-7-carboxamide;

N-(4-fluorobenzyl)-8-hydroxy-5-(1-oxido-5-oxo-1,4-thiazepan-7-yl)-[1,6]naphthyridine-7-carboxamide;

N-(4-fluorobenzyl)-8-hydroxy-5-(1,1-dioxido-5-oxo-1,4-thiazepan-7-yl)[1,6]-naphthyridine-7-carboxamide;

N-(4-fluorobenzyl)-5-{[2-(dimethylamino)-2-oxoethyl]sulfanyl}-8-hydroxy-[1,6]napthyridine-7-carboxamide;

N-(4-fluorobenzyl)-5-[2-(dimethylamino)-2-oxoethoxy]-8-hydroxy-[1,6]napthyridine-7-carboxamide;

N-(4-fluorobenzyl)-5-{[2-(dimethylamino)-2-oxoethyl](methylsulfonyl)amino}-8-hydroxy-[1,6]napthyridine-7-carboxamide;

N-(4-fluorobenzyl)-5-[3-(dimethylamino)-3-oxopropyl]-8-hydroxy-[1,6]napthyridine-7-carboxamide;

N-(4-fluorobenzyl)-5-[(1*E*)-3-(dimethylamino)-3-oxo-1-propenyl]-8-hydroxy-[1,6]napthyridine-7-carboxamide;

N-(4-fluorobenzyl)-5-[2-(3-oxo-1-piperazinyl)ethyl]-8-hydroxy-[1,6]napthyridine-7-carboxamide;

N-(4-fluorobenzyl)-5-[2-(2-oxo-1-imidazolidinyl)ethyl]-8-hydroxy-[1,6]napthyridine-7-carboxamide;

N-(4-fluorobenzyl)-5-[2-(2-oxo-1-piperazinyl)ethyl]-8-hydroxy-[1,6]napthyridine-7-carboxamide;

5-(1,1-dioxido-1,2-thiazinan-2-yl)-*N*-(4-fluorobenzyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide;

5-(1,1-dioxidoisothiazolidin-2-yl)-*N*-(4-fluorobenzyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide;

N-(4-fluorobenzyl)-8-hydroxy-5-[methyl(methylsulfonyl)amino]-1,6-naphthyridine-7-carboxamide;

5-[acetyl(methyl)amino]-*N*-(4-fluorobenzyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide;

5-[[(dimethylamino)carbonyl](methyl)amino]-*N*-(4-fluorobenzyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide;

N-(4-fluorobenzyl)-6-hydroxy-3-methyl-1-(2-morpholin-4-ylethyl)-2-oxo-2,3-dihydro-1H-pyrimido[4,5,6-de]-1,6-naphthyridine-5-carboxamide;

N-(4-fluorobenzyl)-8-hydroxy-5-thiomorpholin-4-yl-1,6-naphthyridine-7-carboxamide;

5-(1,1-dioxidothiomorpholin-4-yl)-*N*-(4-fluorobenzyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide;

N-(4-fluorobenzyl)-8-hydroxy-5-(4-methyl-3-oxopiperazin-1-yl)-1,6-naphthyridine-7-carboxamide;

1-(7-{[4-fluorobenzyl)amino]carbonyl}-8-hydroxy-1,6-naphthyridin-5-yl-L-prolinamide;

N-(4-fluorobenzyl)-8-hydroxy-5-(2-oxotetrahydropyrimidin-1(2*H*)-yl)-1,6-naphthyridine-7-carboxamide;

N-(4-fluorobenzyl)-8-hydroxy-5-(2-oxoimidazolidin-1-yl)-1,6-naphthyridine-7-carboxamide;

N-7-(4-fluorobenzyl)-8-hydroxy-*N* 5, *N* 5-dimethyl-1,6-naphthyridine-5,7-dicarboxamide;

N 7-(4-fluorobenzyl)-8-hydroxy-*N* 5-isopropyl-*N* 5-methyl-1,6-naphthyridine-5,7-dicarboxamide;

N 7-(4-fluorobenzyl)-8-hydroxy-*N* 5-(2-morpholin-4-ylethyl)-1,6-naphthyridine-5,7-dicarboxamide;

N 5-[2-(dimethylamino)-2-oxoethyl]-*N* 7-(4-fluorobenzyl)-8-hydroxy-*N* 5-methyl-1,6-naphthyridine-5,7-dicarboxamide;

N-(4-fluorobenzyl)-5-(1,1-dioxido-4-oxo-1,2,5-thiadiazepan-2-yl)-8-hydroxy-[1,6]napthyridine-7-carboxamide;

and pharmaceutically acceptable salts thereof.

In still another aspect, the present invention is a compound selected from the group consisting of

N-(4-fluorobenzyl)-5-(1,1-dioxido-5-methyl-4-oxo-1,2,5-thiadiazepan-2-yl)-8-hydroxy-[1,6]napthyridine-7-carboxamide;

N-(4-fluorobenzyl)-5-(1,1-dioxido-5-ethyl-4-oxo-1,2,5-thiadiazepan-2-yl)-8-hydroxy-[1,6]napthyridine-7-carboxamide;

N-(4-fluorobenzyl)-5-(1,1-dioxido-1,5,2-dithiazepan-2-yl)-8-hydroxy-[1,6]napthyridine-7-carboxamide;

N-(4-fluorobenzyl)-5-(1,1,5,5-tetraoxido-1,5,2-dithiazepan-2-yl)-8-hydroxy-[1,6]napthyridine-7-carboxamide;

N-(4-fluorobenzyl)-5-(1,4-dimethyl-7-oxo-1,4-diazepan-5-yl)-8-hydroxy-[1,6]-napthyridine-7-carboxamide;

N-(4-fluorobenzyl)-5-(1-methyl-7-oxo-1,4-diazepan-5-yl)-8-hydroxy-[1,6]-napthyridine-7-carboxamide;

N-(4-Fluorobenzyl)-5-(7-oxo-1,4-diazepan-5-yl)-8-hydroxy-[1,6]-napthyridine-7-carboxamide

N-(4-fluorobenzyl)-5-[4-(methylsulfonyl)thiomorpholin-2-yl]-8-hydroxy-[1,6]napthyridine-7-carboxamide;

N-(4-fluorobenzyl)-5-[4-(methylsulfonyl)-1-oxidothiomorpholin-2-yl]-8-hydroxy-[1,6]napthyridine-7-carboxamide;

N-(4-fluorobenzyl)-5-[4-(methylsulfonyl)-1,1-dioxidothiomorpholin-2-yl]-8-hydroxy-[1,6]napthyridine-7-carboxamide;

N-(4-fluorobenzyl)-5-(2-Acetyl-1-methylpyrazolidin-3-yl)-8-hydroxy-[1,6]napthyridine-7-carboxamide;

N-(4-fluorobenzyl)-5-(1,1-dioxido-1,2,5-thiadiazepan-2-yl)-8-hydroxy-[1,6]napthyridine-7-carboxamide;

N-(4-fluorobenzyl)-8-hydroxy-5-[5-(methylsulfonyl)-1,1-dioxido-1,2,5-thiadiazepan-2-yl]-1,6-naphthyridine-7-carboxamide;

N-(4-fluorobenzyl)-8-hydroxy-5(6-methyl-1,1-dioxido-1,2,6-thiadiazinan-2yl)-1,6-naphthyridine-7-carboxamide;

N-(4-fluorobenzyl)-8-hydroxy-5-{methyl[(1-methyl-1*H*-imidazol-4-yl)sulfonyl]amino}-1,6-naphthyridine-7-carboxamide;

N-[4-fluoro-2-(methylsulfonyl)benzyl]-8-hydroxy-5-{methyl[(1-methyl-1*H*-imidazol-4-yl)sulfonyl]amino}-1,6-naphthyridine-7-carboxamide;

N-7-[4-fluoro-2-(methylsulfonyl)benzyl]-8-hydroxy-N-5-,N-5-dimethyl-1,6-naphthyridine-5,7-dicarboxamide;

N-[4-fluoro-2-(methylsulfonyl)benzyl]-8-hydroxy-5-(1,1-dioxido-1,2-thiazinan-2-yl)-1,6-naphthyridine-7-carboxamide

N-(2-(methylsulfonyl)benzyl)-5-(1,1-dioxido-1,2-thiazinan-2-yl)-8-hydroxy-1,6-naphthyridine-7-carboxamide;

N-(2-[(dimethylaminosulfonyl]-4-fluorobenzyl)-5-(1,1-dioxido-1,2-thiazinan-2-yl)-8-hydroxy-1,6-naphthyridine-7-carboxamide;

N-(4-fluorobenzyl)-8-hydroxy-5-(1-methyl-5-oxopyrrolidin-3-yl)-1,6-naphthyridine-7-carboxamide;

and pharmaceutically acceptable salts thereof.

Other embodiments of the present invention include the following:

(a) A pharmaceutical composition comprising a compound of Formula (I) and a pharmaceutically acceptable carrier.

(b) The pharmaceutical composition of (a), further comprising at least one antiviral selected from the group consisting of HIV protease inhibitors, non-nucleoside HIV reverse transcriptase inhibitors, and nucleoside HIV reverse transcriptase inhibitors.

(c) A method of inhibiting HIV integrase in a subject in need thereof which comprises administering to the subject a therapeutically effective amount of a compound of Formula (I).

(d) A method of preventing or treating infection by HIV in a subject in need thereof which comprises administering to the subject a therapeutically effective amount of a compound of Formula (I).

(e) The method of (d), wherein the compound of Formula (I) is administered in combination with a therapeutically effective amount of at least one antiviral selected from the group consisting of HIV protease inhibitors, non-nucleoside HIV reverse transcriptase inhibitors, and nucleoside HIV reverse transcriptase inhibitors.

(f) A method of preventing, treating or delaying the onset of AIDS in a subject in need thereof which comprises administering to the subject a therapeutically effective amount of a compound of Formula (I).

(g) The method of (f), wherein the compound is administered in combination with a therapeutically effective amount of at least one antiviral selected from the group consisting of HIV protease inhibitors, non-nucleoside HIV reverse transcriptase inhibitors, and nucleoside HIV reverse transcriptase inhibitors

(h) A method of inhibiting HIV integrase in a subject in need thereof which comprises administering to the subject a therapeutically effective amount of the composition of (a) or (b).

(i) A method of preventing or treating infection by HIV in a subject in need thereof which comprises administering to the subject a therapeutically effective amount of the composition of (a) or (b).

(j) A method of preventing, treating or delaying the onset of AIDS in a subject in need thereof which comprises administering to the subject a therapeutically effective amount of the composition of (a) or (b).

Still other embodiments of the present invention include the following:

(k) A pharmaceutical composition which comprises the product prepared by combining (e.g., mixing) an effective amount of a compound of Formula (I) and a pharmaceutically acceptable carrier.

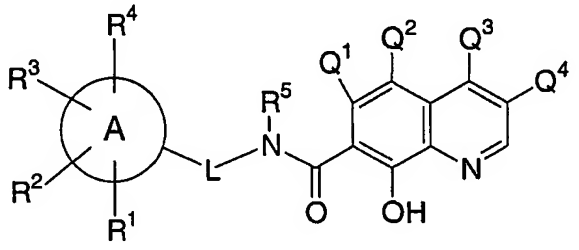
(l) A combination useful for inhibiting HIV integrase, for treating or preventing infection by HIV, or for preventing, treating or delaying the onset of AIDS, which is a therapeutically effective amount of a compound of Formula (I) and a therapeutically effective amount of an HIV infection/AIDS treatment agent selected from the group consisting of HIV/AIDS antiviral agents, immunomodulators, and anti-infective agents.

(m) The combination of (l), wherein the HIV infection/AIDS treatment agent is an antiviral selected from the group consisting of HIV protease

inhibitors, non-nucleoside HIV reverse transcriptase inhibitors and nucleoside HIV reverse transcriptase inhibitors.

Additional embodiments of the invention include the pharmaceutical compositions and methods set forth in (a)-(j) above and the compositions and combinations set forth in (k)-(m), wherein the compound employed therein is a compound of one of the embodiments, classes, sub-classes, or aspects of compounds described above. In all of these embodiments, the compound may optionally be used in the form of a pharmaceutically acceptable salt.

The present invention also includes use of a compound of Formula (I-A):



(I-A),

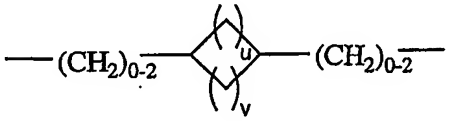
or a pharmaceutically acceptable salt thereof, for inhibiting HIV integrase, for preventing or treating infection by HIV or for preventing, treating or delaying the onset of AIDS in a subject in need thereof; wherein A, R^1, R^2, R^3, R^4, R^5, L, Q^1, Q^2, Q^3, and Q^4 are each independently as originally defined above or as defined in any of the foregoing embodiments, classes, sub-classes, or aspects. In one aspect, the compound of Formula (I-A) is selected from the group consisting of: benzyl 8-hydroxyquinoline-7-carboxamide; 1-methyl-3-phenylpropyl 8-hydroxyquinoline-7-carboxamide; 2-phenylcyclopropyl 8-hydroxyquinoline-7-carboxamide; 1-indanyl 8-hydroxyquinoline-7-carboxamide; N-[(2*E*)-3-phenyl-2-propenyl] 8-hydroxyquinoline-7-carboxamide; benzyl 8-hydroxyquinoline-7-carboxamide; and pharmaceutically acceptable salts thereof.

The present invention also include embodiments for compounds of Formula (I-A) analogous to embodiments (a)-(m) for compounds of Formula (I).

As used herein, the term "C_{1-6} alkyl" (or "C_1-C_6 alkyl") means linear or branched chain alkyl groups having from 1 to 6 carbon atoms and includes all of the hexyl alkyl and pentyl alkyl isomers as well as n-, iso-, sec- and t-butyl, n- and

isopropyl, ethyl and methyl. "C_{1-4} alkyl" means n-, iso-, sec- and t-butyl, n- and isopropyl, ethyl and methyl.

The term "C_0" as employed in expressions such as "C_{0-6} alkyl" means a direct covalent bond. Similarly, when an integer defining the presence of a certain number of ring atoms in a cyclic group is equal to zero, it means that the ring atoms adjacent thereto in the cyclic group are connected directly by a bond. For example, when L is



wherein u and v are each integers having a value from 0 to 4, provided that the sum of u + v is 1, 2, 3 or 4, L has the following structure when u is 1 and v is zero:

The term "C_{2-5} alkenyl" (or "C_2-C_5 alkenyl") means linear or branched chain alkenyl groups having from 2 to 5 carbon atoms and includes all of the pentenyl isomers as well as 1-butenyl, 2-butenyl, 3-butenyl, isobutenyl, 1-propenyl, 2-propenyl, and ethenyl (or vinyl). Similar terms such as "C_{2-3} alkenyl" have an analogous meaning.

The term "C_{2-5} alkynyl" (or "C_2-C_5 alkynyl") means linear or branched chain alkynyl groups having from 2 to 5 carbon atoms and includes all of the pentynyl isomers as well as 1-butynyl, 2-butynyl, 3-butynyl, 1-propynyl, 2-propynyl, and ethynyl (or acetylenyl). Similar terms such as "C_{2-3} alkynyl" have an analogous meaning.

The term "C_{3-7} cycloalkyl" (or "C_3-C_7 cycloalkyl") means a cyclic ring of an alkane having three to seven total carbon atoms (i.e., cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, or cycloheptyl). The term "C_{3-6} cycloalkyl" refers to a cyclic ring selected from cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl. Terms such as "C_3-C_5 cycloalkyl" have an analogous meaning.

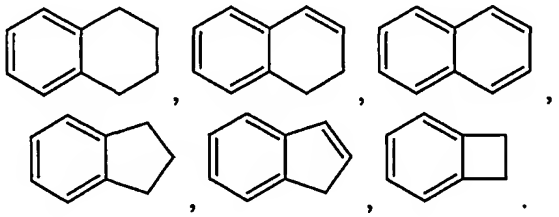
The term "halogen" (or "halo") refers to fluorine, chlorine, bromine and iodine (alternatively, fluoro, chloro, bromo, and iodo).

The term "thio" (also referred to as "thioxo") means divalent sulfur; i.e., =S.

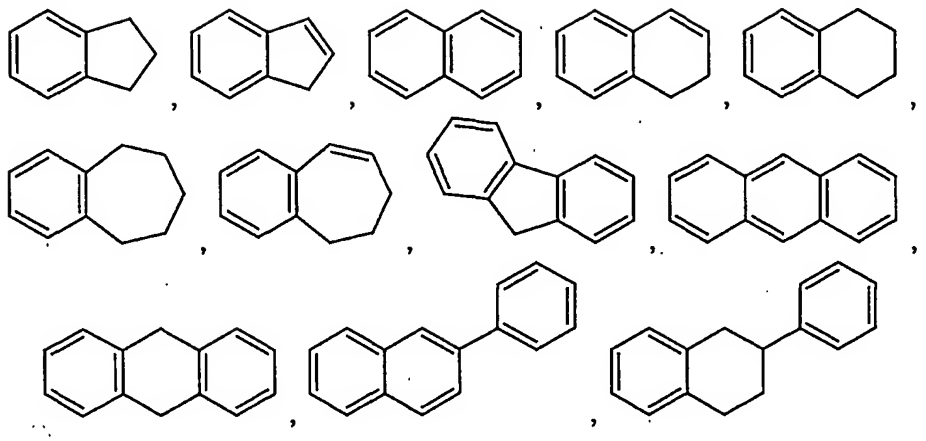
The term "C_{1-6} haloalkyl" (which may alternatively be referred to as "C_1-C_6 haloalkyl" or "halogenated C_1-C_6 alkyl") means a C_1 to C_6 linear or branched alkyl group as defined above with one or more halogen substituents. The term "C_{1-4} haloalkyl" has an analogous meaning.

The term "C_{1-6} fluoroalkyl" (which may alternatively be referred to as "C_1-C_6 fluoroalkyl" or "fluorinated C_1-C_6 alkyl") means a C_1 to C_6 linear or branched alkyl group as defined above with one or more fluorine substituents. The term "C_{1-4} fluoroalkyl" (or "C_1-C_4 fluoroalkyl" or "fluorinated C_1-C_4 alkyl") has an analogous meaning. Representative examples of suitable fluoroalkyls include the series $(CH_2)_{0-4}CF_3$ (i.e., trifluoromethyl, 2,2,2-trifluoroethyl, 3,3,3-trifluoro-n-propyl, etc.), 1-fluoroethyl, 2-fluoroethyl, 2,2-difluoroethyl, 3,3,3-trifluoroisopropyl, 1,1,1,3,3,3-hexafluoroisopropyl, and perfluorohexyl.

The term "carbocycle" (and variations thereof such as "carbocyclic" or "carbocyclyl") as used herein broadly refers to a C_3 to C_8 monocyclic, saturated or unsaturated ring or a C_7 to C_{12} bicyclic ring system in which the rings are independent or fused and in which each ring is saturated or unsaturated. The carbocycle may be attached at any carbon atom which results in a stable compound. The fused bicyclic carbocycles are a subset of the carbocycles; i.e., the term "fused bicyclic carbocycle" generally refers to a C_7 to C_{10} bicyclic ring system in which each ring is saturated or unsaturated and two adjacent carbon atoms are shared by each of the rings in the ring system. A subset of the fused bicyclic carbocycles are those bicyclic carbocycles in which one ring is a benzene ring and the other ring is saturated or unsaturated, with attachment via any carbon atom that results in a stable compound. Representative examples of this subset include the following:



As used herein, the term "fused carbocyclic ring system" refers to a carbocycle as defined above which is fused to a phenyl ring. Representative examples include:



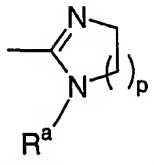
The term "aryl" refers to aromatic mono- and poly-carbocyclic ring systems, wherein the individual carbocyclic rings in the polyring systems may be fused or attached to each other via a single bond. Suitable aryl groups include, but are not limited to, phenyl, naphthyl, and biphenylenyl.

The term "heterocycle" (and variations thereof such as "heterocyclic" or "heterocyclyl") broadly refers to a 4- to 8-membered monocyclic ring, 7- to 12-membered bicyclic ring system, or an 11 to 16-membered tricyclic ring system, any ring of which is saturated or unsaturated, and which consists of carbon atoms and one or more heteroatoms selected from N, O and S, and wherein the nitrogen and sulfur heteroatoms may optionally be oxidized, and the nitrogen heteroatom may optionally be quaternized. The heterocyclic ring may be attached at any heteroatom or carbon atom, provided that attachment results in the creation of a stable structure. When the heterocyclic ring has substituents, it is understood that the substituents may be attached to any atom in the ring, whether a heteroatom or a carbon atom, provided that a stable chemical structure results. Representative examples of heterocyclics include piperidinyl, piperazinyl, azepinyl, pyrrolyl, pyrrolidinyl, pyrazolyl, pyrazolidinyl, imidazolyl, imidazolidinyl, triazolyl, tetrazolyl, imidazolinyl, pyridyl (or pyridinyl), pyrazinyl, pyrimidinyl, pyridazinyl, oxazolyl, oxazolidinyl, isoxazolyl, isoxazolidinyl, morpholinyl, thiomorpholinyl, thiazolyl, thiazolidinyl, isothiazolyl, quinoxazolinyl, isothiazolidinyl, quinolinyl, isoquinolinyl, benzimidazolyl, thiadazolyl, benzopyranyl, benzothiazolyl, benzoazolyl, furyl (or furanyl), tetrahydrofuryl (or tetrahydrofuranyl), tetrahydropuranyl, thienyl (alternatively thiophenyl), benzothiophenyl, oxadiazolyl, and benzo-1,3-dioxacyclopentyl

(alternatively, 1,3-benzodioxolyl). Representative examples of heterocyclics also include tetrahydrothienyl, tetrahydrodioxothienyl, thiadiazinanyl, dioxothiadiazinanyl, thiazinanyl, dioxothiazinanyl, dioxothiazolidinyl, and isodioxothiazolidinyl. Representative examples of heterocyclics also include the following bicyclics: indolyl, benzotriazolyl, imidazo[4,5-b]pyridinyl, dihydroimidazo[4,5-b]pyridinyl, pyrazolo[4,3-c]pyridinyl, dihydropyrazolo[4,3-c]pyridinyl, tetrahydropyrazolo[4,3-c]pyridinyl, pyrrolo[1,2-a]pyrazinyl, dihydropyrrolo[1,2-a]pyrazinyl, tetrahydropyrrolo[1,2-a]pyrazinyl, octahydropyrrolo[1,2-a]pyrazinyl, isoindolyl, indazolyl, indolinyl, isoindolinyl, quinoxalinyl, quinazolinyl, cinnolinyl, chromanyl, and isochromanyl. Additional representative examples of bicyclics include the following: phthalazinyl, purinyl, 1,6-naphthyridinyl, 1,8-napthyridinyl, dihydroindolyl, dihydroisoindolyl, tetrahydroquinolyl, tetrahydroisoquinolyl, imidazo[1,2-*a*]pyrimidinyl, 2,3-dihydroimidazo[2,1-*b*][1,3]thiazolyl, benzazepinyl, dihydrobenazepinyl, benzodiazepinyl, dihydrobenzodiazepinyl, and tetrahydrobenzodiazepinyl. Representative examples of heterocyclics also include the following tricyclics: phenothiazinyl, carbazolyl, beta-carbolinyl, tetrahydro-beta-carbolinyl, acridinyl, phenazinyl, and phenoxazinyl.

Representative examples of heterocyclics also include the following saturated monocyclics: hexahydropyrimidinyl, thiazinanyl (e.g., 1,2-thiazinanyl, alternatively named tetrahydro-1,2-thiazinyl), thiazepanyl (e.g., 1,4-thiazepanyl, alternatively named hexahydro-1,4-thiazepinyl), azepanyl (alternatively hexahydroazepinyl), thiadiazepanyl (e.g., 1,2,5-thiadiazepanyl), dithiazepanyl (e.g., , 1,5,2,-dithiazepanyl), diazepanyl (e.g., 1,4-diazepanyl), and thiadiazinanyl (e.g., 1,2,6-thiadiazinanyl).

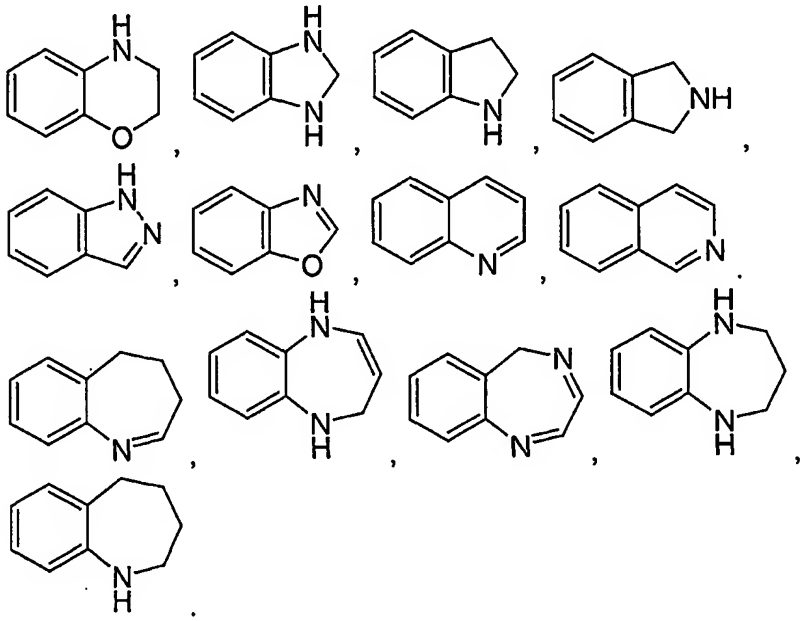
A representative unsaturated heterocycle is



, wherein p is an integer from zero to 4 and R^a is as defined above, and wherein each ring carbon is optionally and independently substituted with -C_{1-4} alkyl.

Representative examples of heterocyclics also include the following bicyclics: hexahydropyrazolo[4,3-c]pyridinyl (e.g., 3a,4,5,6,7,7a-hexahydro-1H-pyrazolo[4,3c]pyridinyl), hexahydropurinyl (e.g., 2,3,4,5,6,7-hexahydro-1H-purinyl), hexahydrooxazolo[3,4a]pyrazinyl, and 1,2,3,4-tetrahydro-1,8-naphthyridinyl.

Fused ring heterocycles form a subset of the heterocycles as defined above; e.g., the term "fused bicyclic heterocycle" refers to a heteroatom-containing bicyclic ring system as defined in the preceding paragraph in which two adjacent atoms are shared by both rings. A subset of the fused bicyclic heterocycles is the fused bicyclic heterocycle containing carbon atoms and one or more heteroatoms selected from nitrogen, oxygen and sulfur, wherein one ring is a benzene ring and the other is a saturated or unsaturated heteroatom-containing ring. Representative examples of this subset include, but are not limited to, the following:



The term "heteromonocycle" (and variations thereof such as "heteromonocyclyl" or "heteromonocyclic") refers to a 4- to 8-membered monocyclic ring which is saturated or unsaturated, and which consists of carbon atoms and one or more heteroatoms selected from N, O and S, and wherein the nitrogen and sulfur heteroatoms may optionally be oxidized, and the nitrogen heteroatom may optionally be quaternized. The heterocyclic ring may be attached at any heteroatom or carbon atom, provided that attachment results in the creation of a stable structure. Representative examples of monoheterocycles are disclosed above.

Heteroaromatics form another subset of the heterocycles as defined above; i.e., the term "heteroaromatic" (alternatively "heteroaryl") generally refers to a

heterocycle as defined above in which the ring system (whether mono- or poly-cyclic) is an aromatic ring system. The term "heteroaromatic ring" refers to a monocyclic heterocycle as defined above which is an aromatic heterocycle. Representative examples of heteroaromatics include pyridyl, pyrrolyl, pyrazinyl, pyrimidinyl, pyridazinyl, thienyl (or thiophenyl), thiazolyl, furanyl, imidazolyl, pyrazolyl, triazolyl, tetrazolyl, oxazolyl, isooxazolyl, oxadiazolyl, thiazolyl, isothiazolyl, and thiadiazolyl.

Unless expressly set forth to the contrary, an "unsaturated" ring is a partially or fully unsaturated ring. For example, an "unsaturated monocyclic C_6 carbocycle" refers to cyclohexene, cyclohexadiene, and benzene.

The present invention includes pharmaceutical compositions useful for inhibiting HIV integrase, comprising an effective amount of a compound of this invention, and a pharmaceutically acceptable carrier. Pharmaceutical compositions useful for treating infection by HIV, or for treating AIDS or ARC, are also encompassed by the present invention, as well as a method of inhibiting HIV integrase, and a method of treating infection by HIV, or of treating AIDS or ARC. Additionally, the present invention is directed to a pharmaceutical composition comprising a therapeutically effective amount of a compound of the present invention in combination with a therapeutically effective amount of an agent for treating HIV infection or AIDS selected from:

(1) an antiviral agent useful for treating or preventing HIV infection or for treating AIDS (also referred to herein as an HIV/AIDS antiviral agent),

(2) an anti-infective agent, and

(3) an immunomodulator.

The present invention also includes a compound of the present invention for use in (a) inhibiting HIV protease, (b) preventing or treating infection by HIV, or (c) preventing, treating or delaying the onset of AIDS or ARC. The present invention also includes the use of a compound of the present invention as described above as a medicament for (a) inhibiting HIV integrase, (b) preventing or treating infection by HIV, or (c) preventing, treating or delaying the onset of AIDS or ARC. The present invention further includes the use of any of the HIV integrase inhibiting compounds of the present invention as described above in combination with one or more HIV/AIDS treatment agents selected from an HIV/AIDS antiviral agent, an anti-

infective agent, and an immunomodulator as a medicament for (a) inhibiting HIV integrase, (b) preventing or treating infection by HIV, or (c) preventing, treating or delaying the onset of AIDS or ARC, said medicament comprising an effective amount of the HIV integrase inhibitor compound and an effective amount of the one or more treatment agents.

The present invention also includes the use of a compound of the present invention as described above in the preparation of a medicament for (a) inhibiting HIV integrase, (b) preventing or treating infection by HIV, or (c) preventing, treating or delaying the onset of AIDS or ARC.

The present invention further includes the use of any of the HIV integrase inhibiting compounds of the present invention as described above in combination with one or more HIV/AIDS treatment agents selected from an HIV/AIDS antiviral agent, an anti-infective agent, and an immunomodulator for the manufacture of a medicament for (a) inhibiting HIV integrase, (b) preventing or treating infection by HIV, or (c) preventing, treating or delaying the onset of AIDS or ARC, said medicament comprising an effective amount of the HIV integrase inhibitor compound and an effective amount of the one or more treatment agents.

The compounds of the present invention may have asymmetric centers and may occur, except when specifically noted, as mixtures of stereoisomers or as individual diastereomers, or enantiomers, with all isomeric forms being included in the present invention.

When any variable (e.g., R^a, R^b, R^c, R^k, etc.) occurs more than one time in any constituent or in Formula I or in any other formula depicting and describing compounds of the invention, its definition on each occurrence is independent of its definition at every other occurrence. Also, combinations of substituents and/or variables are permissible only if such combinations result in stable compounds.

The term "substituted" (e.g., as in "phenyl ring, unsubstituted or substituted with from 1 to 5 substituents ...") includes mono- and poly-substitution by a named substituent to the extent such single and multiple substitution is chemically allowed. For example, a carbocycle or heterocycle substituted with more than one substituent can have multiple substituents on the same ring atom to the extent it is chemically permitted. A ring sulfur atom in a saturated heterocycle can, for example, typically be substituted with 1 (-S(=O)-) or 2 oxo groups ($-SO_2-$).

The compounds of the present inventions are useful in the inhibition of HIV integrase, the prevention or treatment of infection by human immunodeficiency virus (HIV) and the treatment of consequent pathological conditions such as AIDS. Treating AIDS or preventing or treating infection by HIV is defined as including, but not limited to, treating a wide range of states of HIV infection: AIDS, ARC (AIDS related complex), both symptomatic and asymptomatic, and actual or potential exposure to HIV. For example, the compounds of this invention are useful in treating infection by HIV after suspected past exposure to HIV by e.g., blood transfusion, exchange of body fluids, bites, accidental needle stick, or exposure to patient blood during surgery.

The compounds of this invention are useful in the preparation and execution of screening assays for antiviral compounds. For example, the compounds of this invention are useful for isolating enzyme mutants, which are excellent screening tools for more powerful antiviral compounds. Furthermore, the compounds of this invention are useful in establishing or determining the binding site of other antivirals to HIV integrase, e.g., by competitive inhibition. Thus the compounds of this invention are commercial products to be sold for these purposes.

The present invention also provides for the use of a compound of Formula (I) or (I-A) to make a pharmaceutical composition useful for inhibiting HIV integrase and in the treatment of AIDS or ARC.

The compounds of the present invention may be administered in the form of pharmaceutically acceptable salts. The term "pharmaceutically acceptable salt" is intended to include all acceptable salts such as acetate, lactobionate, benzenesulfonate, laurate, benzoate, malate, bicarbonate, maleate, bisulfate, mandelate, bitartrate, mesylate, borate, methylbromide, bromide, methylnitrate, calcium edetate, methylsulfate, camsylate, mucate, carbonate, napsylate, chloride, nitrate, clavulanate, N-methylglucamine, citrate, ammonium salt, dihydrochloride, oleate, edetate, oxalate, edisylate, pamoate (embonate), estolate, palmitate, esylate, pantothenate, fumarate, phosphate/diphosphate, gluceptate, polygalacturonate, gluconate, salicylate, glutamate, stearate, glycollylarsanilate, sulfate, hexylresorcinate, subacetate, hydrabamine, succinate, hydrobromide, tannate, hydrochloride, tartrate, hydroxynaphthoate, teoclate, iodide, tosylate, isothionate, triethiodide, lactate, panoate, valerate, and the like which can be used as a dosage form for modifying the solubility or hydrolysis characteristics or can be used in sustained release or pro-drug

formulations. Depending on the particular functionality of the compound of the present invention, pharmaceutically acceptable salts of the compounds of this invention include those formed from cations such as sodium, potassium, aluminum, calcium, lithium, magnesium, zinc, and from bases such as ammonia, ethylenediamine, N-methyl-glutamine, lysine, arginine, ornithine, choline, N,N'-dibenzylethylene-diamine, chloroprocaine, diethanolamine, procaine, N-benzylphenethyl-amine, diethylamine, piperazine, tris(hydroxymethyl)aminomethane, and tetramethylammonium hydroxide. These salts may be prepared by standard procedures, e.g. by reacting a free acid with a suitable organic or inorganic base. Where a basic group is present, such as amino, an acidic salt, i.e. hydrochloride, hydrobromide, acetate, pamoate, and the like, can be used as the dosage form.

Also, in the case of an acid (-COOH) or alcohol group being present, pharmaceutically acceptable esters can be employed, e.g. acetate, maleate, pivaloyloxymethyl, and the like, and those esters known in the art for modifying solubility or hydrolysis characteristics for use as sustained release or prodrug formulations.

For these purposes, the compounds of the present invention may be administered orally, parenterally (including subcutaneous injections, intravenous, intramuscular, intrasternal injection or infusion techniques), by inhalation spray, or rectally, in dosage unit formulations containing conventional non-toxic pharmaceutically-acceptable carriers, adjuvants and vehicles.

The term "administration" and variants thereof (e.g., "administering" a compound) in reference to a compound of the invention each mean providing the compound or a prodrug of the compound to the individual in need of treatment. When a compound of the invention or prodrug thereof is provided in combination with one or more other active agents (e.g., antiviral agents useful for treating HIV infection or AIDS), "administration" and its variants are each understood to include concurrent and sequential provision of the compound or prodrug thereof and other agents.

Thus, in accordance with the present invention there is further provided a method of treating and a pharmaceutical composition for treating HIV infection and AIDS. The treatment involves administering to a subject in need of such treatment a pharmaceutical composition comprising a pharmaceutical carrier and a therapeutically-effective amount of a compound of the present invention.

As used herein, the term "composition" is intended to encompass a product comprising the specified ingredients in the specified amounts, as well as any product which results, directly or indirectly, from combining the specified ingredients in the specified amounts.

By "pharmaceutically acceptable" is meant the carrier, diluent or excipient must be compatible with the other ingredients of the formulation and not deleterious to the recipient thereof.

The term "subject," (alternatively referred to herein as "patient") as used herein refers to an animal, preferably a mammal, most preferably a human, who has been the object of treatment, observation or experiment.

The term "therapeutically effective amount" as used herein means that amount of active compound or pharmaceutical agent that elicits the biological or medicinal response in a tissue, system, animal or human that is being sought by a researcher, veterinarian, medical doctor or other clinician, which includes alleviation of the symptoms of the disease being treated. When the active compound (i.e., active ingredient) is administered as the salt, references to the amount of active ingredient are to the free acid or free base form of the compound.

These pharmaceutical compositions may be in the form of orally-administrable suspensions or tablets or capsules, nasal sprays, sterile injectible preparations, for example, as sterile injectible aqueous or oleagenous suspensions or suppositories.

When administered orally as a suspension, these compositions are prepared according to techniques well-known in the art of pharmaceutical formulation and may contain microcrystalline cellulose for imparting bulk, alginic acid or sodium alginate as a suspending agent, methylcellulose as a viscosity enhancer, and sweeteners/flavoring agents known in the art. As immediate release tablets, these compositions may contain microcrystalline cellulose, dicalcium phosphate, starch, magnesium stearate and lactose and/or other excipients, binders, extenders, disintegrants, diluents and lubricants known in the art.

When administered by nasal aerosol or inhalation, these compositions are prepared according to techniques well-known in the art of pharmaceutical formulation and may be prepared as solutions in saline, employing benzyl alcohol or other suitable preservatives, absorption promoters to enhance bioavailability, fluorocarbons, and/or other solubilizing or dispersing agents known in the art.

The injectible solutions or suspensions may be formulated according to known art, using suitable non-toxic, parenterally-acceptable diluents or solvents, such as mannitol, 1,3-butanediol, water, Ringer's solution or isotonic sodium chloride solution, or suitable dispersing or wetting and suspending agents, such as sterile, bland, fixed oils, including synthetic mono- or diglycerides, and fatty acids, including oleic acid.

When rectally administered in the form of suppositories, these compositions may be prepared by mixing the drug with a suitable non-irritating excipient, such as cocoa butter, synthetic glyceride esters of polyethylene glycols, which are solid at ordinary temperatures, but liquefy and/or dissolve in the rectal cavity to release the drug.

The compounds of this invention can be administered orally to humans in a dosage range of 0.1 to 1000 mg/kg body weight in divided doses. One preferred dosage range is 0.1 to 200 mg/kg body weight orally in divided doses. Another preferred dosage range is 0.5 to 100 mg/kg body weight orally in divided doses. For oral administration, the compositions are preferably provided in the form of tablets containing 1.0 to 1000 milligrams of the active ingredient, particularly 1.0, 5.0, 10.0, 15.0. 20.0, 25.0, 50.0, 75.0, 100.0, 150.0, 200.0, 250.0, 300.0, 400.0, 500.0, 600.0, 750.0, 800.0, 900.0, and 1000.0 milligrams of the active ingredient for the symptomatic adjustment of the dosage to the patient to be treated. It will be understood, however, that the specific dose level and frequency of dosage for any particular patient may be varied and will depend upon a variety of factors including the activity of the specific compound employed, the metabolic stability and length of action of that compound, the age, body weight, general health, sex, diet, mode and time of administration, rate of excretion, drug combination, the severity of the particular condition, and the host undergoing therapy.

The present invention is also directed to combinations of the HIV integrase inhibitor compounds with one or more agents useful in the treatment of HIV infection or AIDS. For example, the compounds of this invention may be effectively administered, whether at periods of pre-exposure and/or post-exposure, in combination with effective amounts of the HIV/AIDS antivirals, imunomodulators, antiinfectives, or vaccines useful for treating HIV infection or AIDS, such as those in the following Table.

ANTIVIRALS

Drug Name	Manufacturer	Indication
Amprenavir 141 W94 GW 141	Glaxo Wellcome	HIV infection, AIDS, ARC (protease inhibitor)
Abacavir GW 1592 1592U89	Glaxo Welcome	HIV infection, AIDS, ARC (reverse transcriptase inhibitor)
Acemannan	Carrington Labs (Irving, TX)	ARC
Acyclovir	Burroughs Wellcome	HIV infection, AIDS, ARC, in combination with AZT
AD-439	Tanox Biosystems	HIV infection, AIDS, ARC
AD-519	Tanox Biosystems	HIV infection, AIDS, ARC
Adefovir dipivoxil	Gilead Sciences	HIV infection
AL-721	Ethigen (Los Angeles, CA)	ARC, PGL, HIV positive, AIDS
Alpha Interferon	Glaxo Wellcome	Kaposi's sarcoma, HIV, in combination w/Retrovir
Ansamycin LM 427	Adria Laboratories (Dublin, OH) Erbamont (Stamford, CT)	ARC
Antibody which neutralizes pH labile alpha aberrant Interferon	Advanced Biotherapy Concepts (Rockville, MD)	AIDS, ARC
AR177	Aronex Pharm	HIV infection, AIDS, ARC
beta-fluoro-ddA	Nat'l Cancer Institute	AIDS-associated diseases

BMS-232623 (CGP-73547)	Bristol-Myers Squibb/ Novartis	HIV infection, AIDS, ARC (protease inhibitor)
BMS-234475 (CGP-61755)	Bristol-Myers Squibb/ Novartis	HIV infection, AIDS, ARC (protease inhibitor)
CI-1012	Warner-Lambert	HIV-1 infection
Cidofovir	Gilead Science	CMV retinitis, herpes, papillomavirus
Curdlan sulfate	AJI Pharma USA	HIV infection
Cytomegalovirus immune globin	MedImmune	CMV retinitis
Cytovene Ganciclovir	Syntex	sight threatening CMV peripheral CMV retinitis
Delaviridine	Pharmacia-Upjohn	HIV infection, AIDS, ARC (protease inhibitor)
Dextran Sulfate	Ueno Fine Chem. Ind. Ltd. (Osaka, Japan)	AIDS, ARC, HIV positive asymptomatic
ddC Dideoxycytidine	Hoffman-La Roche	HIV infection, AIDS, ARC
ddI Dideoxyinosine	Bristol-Myers Squibb	HIV infection, AIDS, ARC; combination with AZT/d4T
mozenavir (DMP-450)	AVID (Camden, NJ)	HIV infection, AIDS, ARC (protease inhibitor)
EL10	Elan Corp, PLC (Gainesville, GA)	HIV infection

Efavirenz (DMP 266) (-) 6-Chloro-4(S)-cyclopropylethynyl-4(S)-trifluoro-methyl-1,4-dihydro-2H-3,1-benzoxazin-2-one,	DuPont (SUSTIVA®), Merck (STOCRIN®)	HIV infection, AIDS, ARC (non-nucleoside RT inhibitor)
Famciclovir	Smith Kline	herpes zoster, herpes simplex
FTC	Emory University	HIV infection, AIDS, ARC (reverse transcriptase inhibitor)
GS 840	Gilead	HIV infection, AIDS, ARC (reverse transcriptase inhibitor)
HBY097	Hoechst Marion Roussel	HIV infection, AIDS, ARC (non-nucleoside reverse transcriptase inhibitor)
Hypericin	VIMRx Pharm.	HIV infection, AIDS, ARC
Recombinant Human Interferon Beta	Triton Biosciences (Almeda, CA)	AIDS, Kaposi's sarcoma, ARC
Interferon alfa-n3	Interferon Sciences	ARC, AIDS
Indinavir	Merck	HIV infection, AIDS, ARC, asymptomatic HIV positive, also in combination with AZT/ddI/ddC
Compound A	Merck	HIV infection, AIDS, ARC, asymptomatic HIV positive
ISIS 2922	ISIS Pharmaceuticals	CMV retinitis
KNI-272	Nat'l Cancer Institute	HIV-assoc. diseases

Lamivudine, 3TC	Glaxo Wellcome	HIV infection, AIDS, ARC (reverse transcriptase inhibitor); also with AZT
Lobucavir	Bristol-Myers Squibb	CMV infection
Nelfinavir	Agouron Pharmaceuticals	HIV infection, AIDS, ARC (protease inhibitor)
Nevirapine	Boeheringer Ingleheim	HIV infection, AIDS, ARC (protease inhibitor)
Novapren	Novaferon Labs, Inc. (Akron, OH)	HIV inhibitor
Peptide T Octapeptide Sequence	Peninsula Labs (Belmont, CA)	AIDS
Trisodium Phosphonoformate	Astra Pharm. Products, Inc	CMV retinitis, HIV infection, other CMV infections
PNU-140690	Pharmacia Upjohn	HIV infection, AIDS, ARC (protease inhibitor)
Probucol	Vyrex	HIV infection, AIDS
RBC-CD4	Sheffield Med. Tech (Houston TX)	HIV infection, AIDS, ARC
Ritonavir (ABT-538)	Abbott	HIV infection, AIDS, ARC (protease inhibitor)
Saquinavir	Hoffmann-LaRoche	HIV infection, AIDS, ARC (protease inhibitor)
Stavudine; d4T Didehydrodeoxy-thymidine	Bristol-Myers Squibb	HIV infection, AIDS, ARC
Valaciclovir	Glaxo Wellcome	genital HSV & CMV infections
Virazole Ribavirin	Viratek/ICN (Costa Mesa, CA)	asymptomatic HIV positive, LAS, ARC
VX-478	Vertex	HIV infection, AIDS, ARC

Zalcitabine	Hoffmann-La Roche	HIV infection, AIDS, ARC, with AZT
Zidovudine; AZT	Glaxo Wellcome	HIV infection, AIDS, ARC, Kaposi's sarcoma in combination with other therapies (reverse transcriptase inhibitor)
ABT-378; Lopinavir	Abbott	HIV infection, AIDS, ARC (protease inhibitor)
ABT-378/r; contains lopinavir and ritonavir; Kaletra	Abbott	HIV infection, AIDS, ARC (protease inhibitor)
JE2147/AG1776	Agouron	HIV infection, AIDS, ARC (protease inhibitor)
T-20	Trimeris	HIV infection, AIDS, ARC (fusion inhibitor)
T-1249	Trimeris	HIV infection, AIDS, ARC (fusion inhibitor)
atazanavir (BMS 232632)	Bristol-Myers-Squibb	HIV infection, AIDS, ARC (protease inhibitor)
PRO 542	Progenics	HIV infection, AIDS, ARC (attachment inhibitor)
PRO 140	Progenics	HIV infection, AIDS, ARC (CCR5 co-receptor inhibitor)
TAK-779	Takeda	HIV infection, AIDS, ARC (injectable CCR5 receptor antagonist)
DPC 681 & DPC 684	DuPont	HIV infection, AIDS, ARC (protease inhibitors)
DPC 961 & DPC 083	DuPont	HIV infection AIDS, ARC (nonnucleoside reverse transcriptase inhibitors)

Trizivir (contains abacavir, lamivudine, and zidovudine)	GlaxoSmithKline	HIV infection, AIDS, ARC (reverse transcriptase inhibitors)
tipranavir (PNU-140690)	Boehringer Ingelheim (purchased from Pharmacia & Upjohn)	HIV infection, AIDS, ARC (protease inhibitor)
tenofovir disoproxil fumarate	Gilead	HIV infection, AIDS, ARC (reverse transcriptase inhibitor)
TMC-120 & TMC-125	Tibotec	HIV infections, AIDS, ARC (non-nucleoside reverse transcriptase inhibitors)
TMC-126	Tibotec	HIV infection, AIDS, ARC (protease inhibitor)

IMMUNO-MODULATORS

Drug Name	Manufacturer	Indication
AS-101	Wyeth-Ayerst	AIDS
Bropirimine	Pharmacia Upjohn	advanced AIDS
Acemannan	Carrington Labs, Inc. (Irving, TX)	AIDS, ARC
CL246,738	American Cyanamid Lederle Labs	AIDS, Kaposi's sarcoma
EL10	Elan Corp, PLC (Gainesville, GA)	HIV infection
FP-21399	Fuki ImmunoPharm	blocks HIV fusion with CD4+ cells
Gamma Interferon	Genentech	ARC, in combination w/TNF (tumor necrosis factor)

Granulocyte Macrophage Colony Stimulating Factor	Genetics Institute Sandoz	AIDS
Granulocyte Macrophage Colony Stimulating Factor	Hoeschst-Roussel Immunex	AIDS
Granulocyte Macrophage Colony Stimulating Factor	Schering-Plough	AIDS, combination w/AZT
HIV Core Particle Immunostimulant	Rorer	seropositive HIV
IL-2 Interleukin-2	Cetus	AIDS, in combination w/AZT
IL-2 Interleukin-2	Hoffman-La Roche Immunex	AIDS, ARC, HIV, in combination w/AZT
IL-2 Interleukin-2 (aldeslukin)	Chiron	AIDS, increase in CD4 cell counts
Immune Globulin Intravenous (human)	Cutter Biological (Berkeley, CA)	pediatric AIDS, in combination w/AZT
IMREG-1	Imreg (New Orleans, LA)	AIDS, Kaposi's sarcoma, ARC, PGL
IMREG-2	Imreg (New Orleans, LA)	AIDS, Kaposi's sarcoma, ARC, PGL
Imuthiol Diethyl Dithio Carbamate	Merieux Institute	AIDS, ARC
Alpha-2 Interferon	Schering Plough	Kaposi's sarcoma w/AZT, AIDS
Methionine-Enkephalin	TNI Pharmaceutical (Chicago, IL)	AIDS, ARC

MTP-PE Muramyl-Tripeptide	Ciba-Geigy Corp.	Kaposi's sarcoma
Granulocyte Colony Stimulating Factor	Amgen	AIDS, in combination w/AZT
Remune	Immune Response Corp.	immunotherapeutic
rCD4 Recombinant Soluble Human CD4	Genentech	AIDS, ARC
rCD4-IgG hybrids		AIDS, ARC
Recombinant Soluble Human CD4	Biogen	AIDS, ARC
Interferon Alfa 2a	Hoffman-La Roche	Kaposi's sarcoma, AIDS, ARC, in combination w/AZT
SK&F106528 Soluble T4	Smith Kline	HIV infection
Thymopentin	Immunobiology Research Institute	HIV infection
Tumor Necrosis Factor; TNF	Genentech	ARC, in combination w/gamma Interferon
etanercept	Immunex Corp (Enbrel®)	rheumatoid arthritis
infliximab	Centocor (Remicade®)	rheumatoid arthritis and Crohn's disease

ANTI-INFECTIVES

Drug Name	Manufacturer	Indication
Clindamycin with Primaquine	Pharmacia Upjohn	PCP
Fluconazole	Pfizer	cryptococcal meningitis, candidiasis

Pastille	Squibb Corp.	prevention of oral candidiasis
Nystatin Pastille		
Ornidyl	Merrell Dow	PCP
Eflornithine		
Pentamidine	LyphoMed	PCP treatment
Isethionate (IM & IV)	(Rosemont, IL)	
Trimethoprim		antibacterial
Trimethoprim/sulfa		antibacterial
Piritrexim	Burroughs Wellcome	PCP treatment
Pentamidine	Fisons Corporation	PCP prophylaxis
isethionate for		
inhalation		
Spiramycin	Rhone-Poulenc	cryptosporidia diarrhea
Intraconazole-	Janssen Pharm.	histoplasmosis; cryptococcal
R51211		meningitis
Trimetrexate	Warner-Lambert	PCP

OTHER

Drug Name	Manufacturer	Indication
Daunorubicin	NeXstar, Sequus	Karposi's sarcoma
Recombinant Human	Ortho Pharm. Corp.	severe anemia assoc. with
Erythropoietin		AZT therapy
Recombinant Human	Serono	AIDS-related wasting,
Growth Hormone		cachexia
Leukotriene B4 Receptor	-	HIV infection
Antagonist		
Megestrol Acetate	Bristol-Myers Squibb	treatment of anorexia assoc. w/AIDS
Soluble CD4 Protein and	-	HIV infection
Derivatives		
Testosterone	Alza, Smith Kline	AIDS-related wasting

Total Enteral Nutrition	Norwich Eaton Pharmaceuticals	diarrhea and malabsorption, related to AIDS

It will be understood that the scope of combinations of the compounds of this invention with HIV/AIDS antivirals, immunomodulators, anti-infectives or vaccines is not limited to the list in the above Table, but includes in principle any combination with any pharmaceutical composition useful for the treatment of HIV infection or AIDS. When employed in combination with the compounds of the invention, the HIV/AIDS antivirals and other agents are typically employed in their conventional dosage ranges and regimens as reported in the art, including the dosages described in the Physicians' Desk Reference, 54th edition, Medical Economics Company, 2000. The dosage ranges for a compound of the invention in these combinations are the same as those set forth above just before the Table.

Preferred combinations are simultaneous or sequential treatments of a compound of the present invention and an inhibitor of HIV protease and/or a non-nucleoside inhibitor of HIV reverse transcriptase. An optional fourth component in the combination is a nucleoside inhibitor of HIV reverse transcriptase, such as AZT, 3TC, ddC or ddI. A preferred inhibitor of HIV protease is the sulfate salt of indinavir, which is N-(2(R)-hydroxy-1(S)-indanyl)-2(R)-phenylmethyl-4-(S)-hydroxy-5-(1-(4-(3-pyridyl-methyl)-2(S)-N'-(t-butylcarboxamido)-piperazinyl))-pentaneamide ethanolate, and is synthesized according to US 5413999. Indinavir is generally administered at a dosage of 800 mg three times a day. Other preferred protease inhibitors are nelfinavir and ritonavir. Another preferred inhibitor of HIV protease is saquinavir which is administered in a dosage of 600 or 1200 mg tid. Still another preferred protease inhibitor is Compound A, which is N-(2(R)-hydroxy-1(S)-indanyl)-2(R)-phenylmethyl-4(S)-hydroxy-5-(1-(4-(2-benzo[b]furanylmethyl)-2(S)-N'-(t-butylcarboxamido)piperazinyl))pentaneamide, preferably administered as the sulfate salt. Compound A can be prepared as described in US 5646148. Preferred non-nucleoside inhibitors of HIV reverse transcriptase include efavirenz. The preparation of ddC, ddI and AZT are also described in EPO 0,484,071. These combinations may have unexpected effects on limiting the spread and degree of infection of HIV. Preferred combinations include a compound of the present invention with the following (1) indinavir with efavirenz, and, optionally, AZT and/or 3TC and/or ddI

and/or ddC; (2) indinavir, and any of AZT and/or ddI and/or ddC and/or 3TC, in particular, indinavir and AZT and 3TC; (3) stavudine and 3TC and/or zidovudine; (4) zidovudine and lamivudine and 141W94 and 1592U89; (5) zidovudine and lamivudine.

Another preferred combination is a compound of the present invention with indinavir and Compound A and optionally with one or more of efavirenz, AZT, 3TC, ddI and ddC. In one embodiment of this combination, the weight ratio of indinavir to Compound A is from about 1:1 to about 1:2, wherein the amount of indinavir employed is in the range of from about 200 to about 1000 mg. Indinavir and Compound A can be administered concurrently or sequentially in either order from one to three times per day.

In such combinations the compound of the present invention and other active agents may be administered together or separately. In addition, the administration of one agent may be prior to, concurrent to, or subsequent to the administration of other agent(s).

Abbreviations used in the instant specification, particularly the Schemes and Examples, include the following:

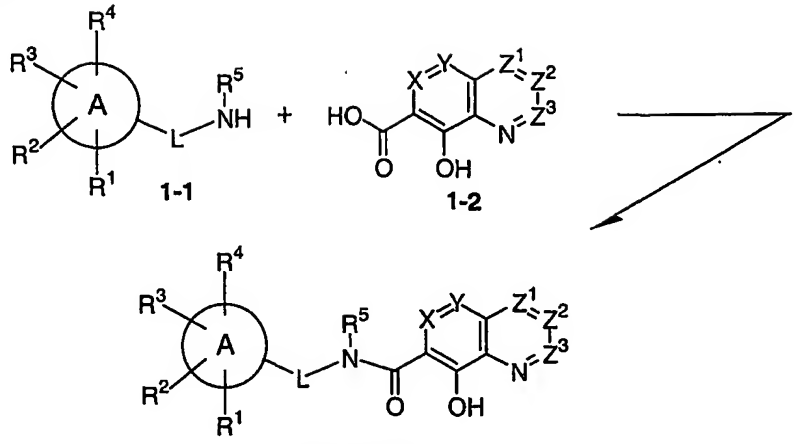
Ac = acetyl
BOP = benzotriazol-1-yloxytris-(dimethylamino)phosphonium hexafluorophosphate
DBU = 1,8-diazabicyclo[5.4.0]undec-7-ene
DEA = diethylamine
DEAD = diethylazodicarboxylate
DMF = N,N-dimethylformamide
DMPU = 1,3-dimethyl-3,4,5,6-tetrahydro-2(1H)-pyrimidinone
DMSO = dimethylsulfoxide
EDC = 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide
EDTA = ethylenediaminetetraacetic acid
ES MS = electrospray mass spectrometry
Et = ethyl

EtOAc = ethyl acetate
EtOH = ethanol
FAB HRMS = fast atom bombardment high resolution mass spectroscopy
FAB MS = fast atom bombardment mass spectroscopy
HOBt = 1-hydroxy benzotriazole hydrate
HPLC = high performance liquid chromatography
i-Pr = isopropyl
Me = methyl
MsCl = methanesulfonyl chloride (or mesyl chloride)
NBS = N-bromosuccinimide
NIS = N-iodosuccinimide
NMR = nuclear magnetic resonance
Ph = phenyl
PMBCl = *p*-methoxybenzyl chloride
rt and RT = room temperature
TFA = trifluoroacetic acid
THF = tetrahydrofuran

The compounds of the present invention can be readily prepared according to the following reaction schemes and examples, or modifications thereof, using readily available starting materials, reagents and conventional synthesis procedures. In these reactions, it is also possible to make use of variants which are themselves known to those of ordinary skill in this art, but are not mentioned in greater detail. Furthermore, other methods for preparing compounds of the invention will be readily apparent to the person of ordinary skill in the art in light of the following reaction schemes and examples. Unless otherwise indicated, all variables are as defined above.

The compounds of the present invention can be prepared by the coupling of suitable (poly)azanaphthenyl carboxylic acids (or acid derivatives such as acid halides or esters) with the appropriate amines, as represented by the following general scheme:

SCHEME 1



Compound I

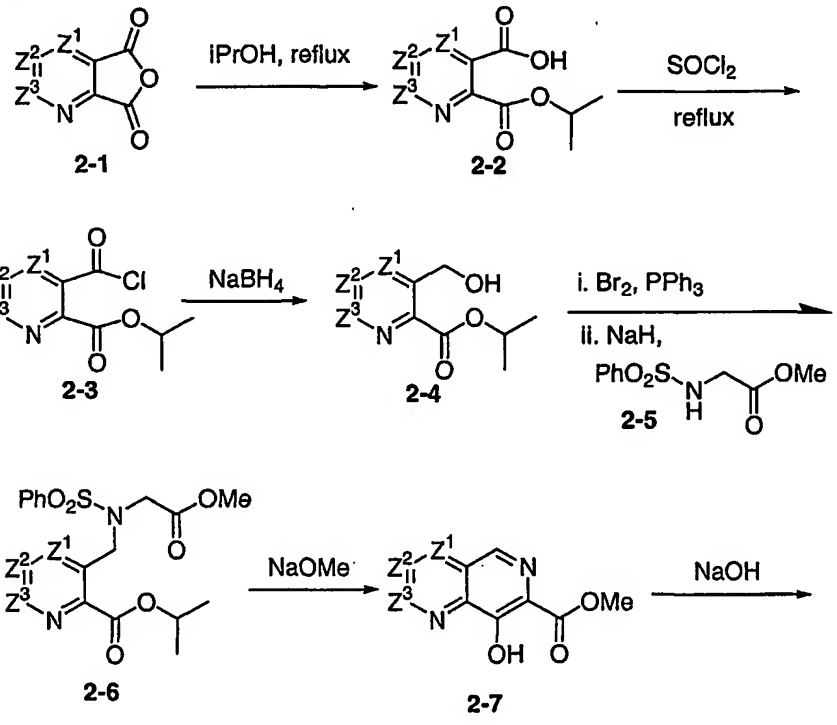
Methods for coupling carboxylic acids with amines to form carboxamides are well known in the art. Suitable methods are described, for example, in Jerry March, Advanced Organic Chemistry, 3rd edition, John Wiley & Sons, 1985, pp. 370-376. Amines of formula **1-1** can be prepared using the methods described in Richard Larock, Comprehensive Organic Transformations, VCH Publishers Inc, 1989, pp 385-438, or routine variations thereof. Azanaphthenyl and polyazanaphthenyl carboxylic acids of formula **1-2** can be prepared using methods described in Ochiai et al., *Chem.Ber.* 1937, 70: 2018, 2023; Albert et al., *J.Chem.Soc.* 1952, 4985, 4991; and Barlin et al., *Aust.J.Chem.* 1990, 43: 1175-1181; or routine variations thereof. Schemes 2-16 below illustrate and expand upon the chemistry portrayed in Scheme 1.

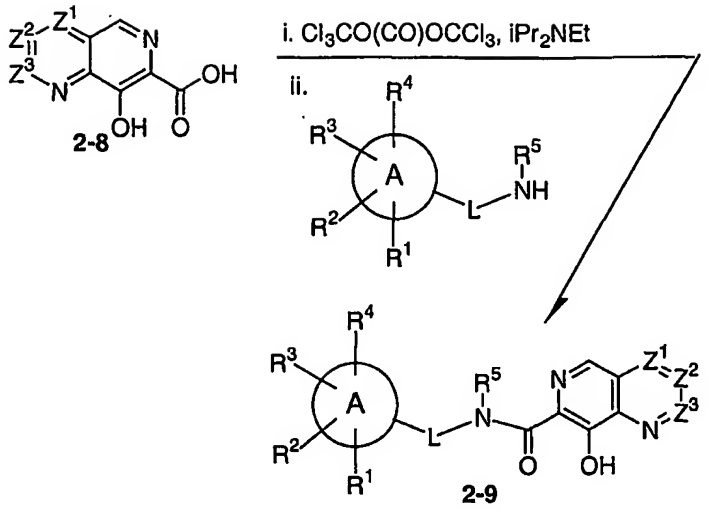
In Scheme 2, following the procedure set forth in Ornstein et al., *J. Med. Chem.* 1989, 32: 827-833, a cyclic anhydride such as quinolinic anhydride (i.e., $Z^1 = Z^2 = Z^3 = CH$ in **2-1**) can be opened with isopropanol to provide mono acid **2-2**, which can be converted to the corresponding acyl chloride **2-3** (e.g., by refluxing thionyl chloride). Acyl chloride **2-3** can then be reduced (e.g., with $NaBH_4$ or $LiBH_4$) to the corresponding alcohol **2-4**, which can be converted to the corresponding bromide through the action of bromine in the presence of triphenylphosphine. Alkylation of the bromide with the sodium anion of phenylsulfonamide **2-5** in a polar aprotic solvent like DMF can provide sulfonamide **2-6**, which can be treated with a base (e.g., alkali metal alkoxide such as sodium methoxide) to provide the bicyclic ester **2-7** via a Dieckmann cyclization.

Saponification of the ester (e.g., with aqueous NaOH at reflux) will afford the acid **2-8**. The acid **2-8** can be activated with triphosgene and coupled with a variety of amines to provide the compounds of the invention **2-9**.

The starting anhydrides of formula **2-1** can be prepared via methods described in Philips et al., *Justus Liebigs Ann. Chem.* 1895, 288: 2535; Bernthsen et al., *Chem.Ber.* 1887; 20: 1209; Bly et al., *J.Org.Chem.* 1964, 29: 2128-2135; and Krapcho et al., *J.Heterocycl.Chem.* 1993, 30: 1597-1606; or routine variations thereof.

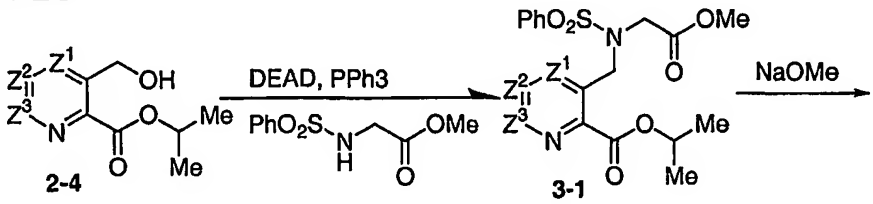
SCHEME 2

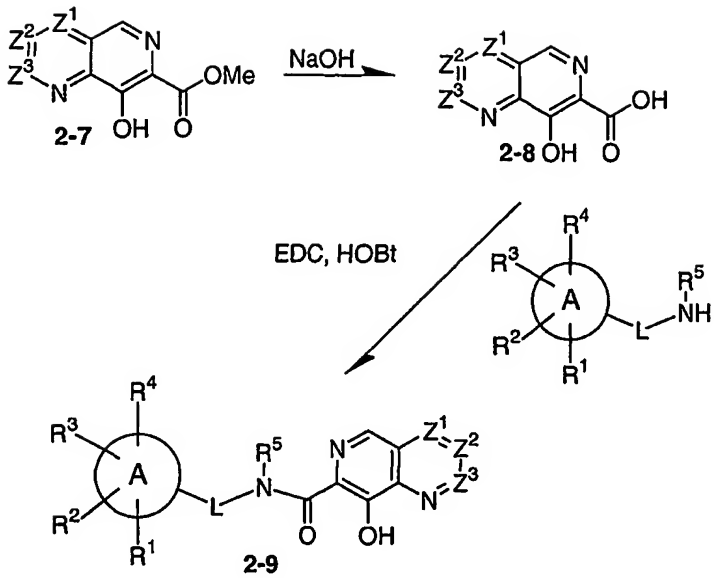




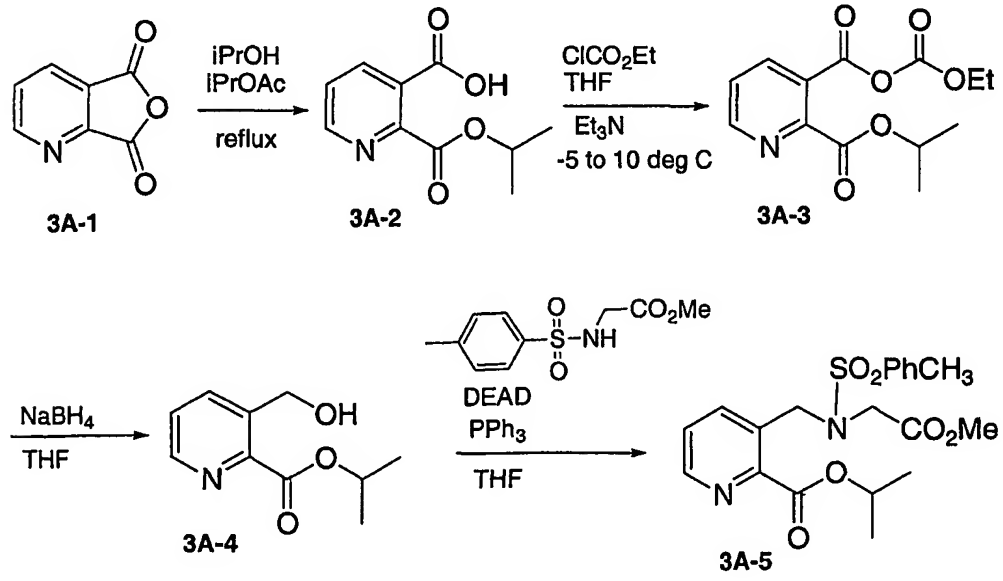
Scheme 3 depicts an alternative synthesis in which alcohol **2-4** can undergo the Mitsunobu reaction with the phenylsulfonamide of glycine methyl ester to provide **3-1**. The sulfonamide **3-1** can again be elaborated to provide the acid **2-8**, which can be coupled with a variety of amines using standard reagents to provide the compounds of the invention **2-9**.

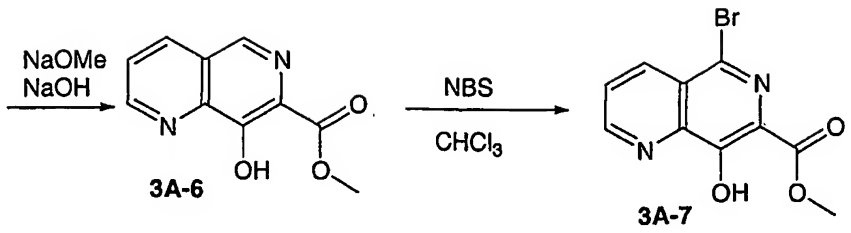
SCHEME 3





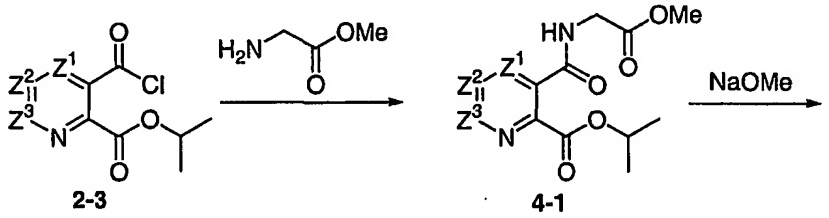
Scheme 3A depicts (for a napthyridine core) a variation of the synthesis shown in Scheme 3, wherein the acid **3A-2** is reacted with ethyl chloroformate to form the mixed anhydride **3A-3**, which is reduced to alcohol **3A-4**.

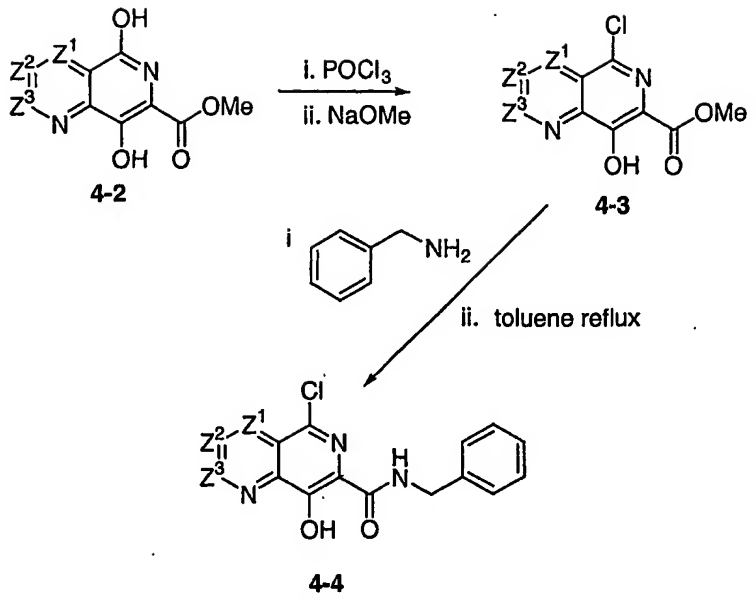




Halogen substituted compounds of the present invention can be prepared as shown in Scheme 4. The acid chloride **2-3** can be reacted with glycine methyl ester to provide the amide **4-1**. Dieckmann cyclization of the ester **4-1** with a sodium alkoxide base in an alcoholic solvent like methanol will provide phenol **4-2**., which can be reacted with phosphorous oxychloride, followed by methanolysis of the intermediate phosphonate esters to provide **4-3**. The ester bond of **4-3** can react selectively with suitable amines in refluxing nonpolar aromatic solvents (e.g., benzylamine refluxed in toluene is depicted in Scheme 4) to provide the corresponding halogenated derivative **4-4**.

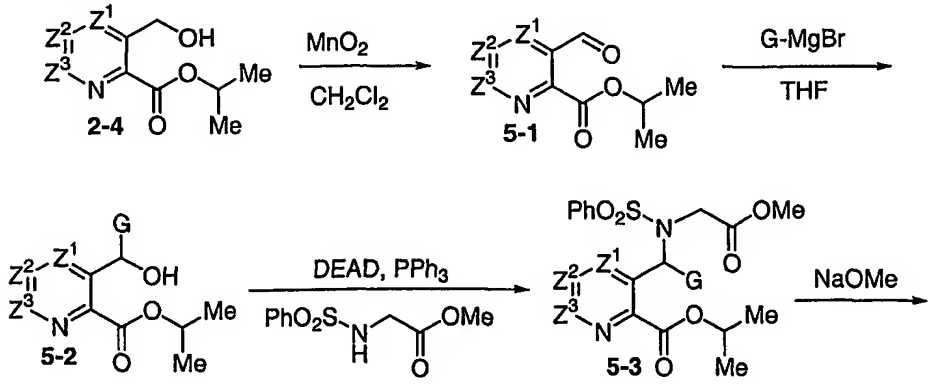
SCHEME 4

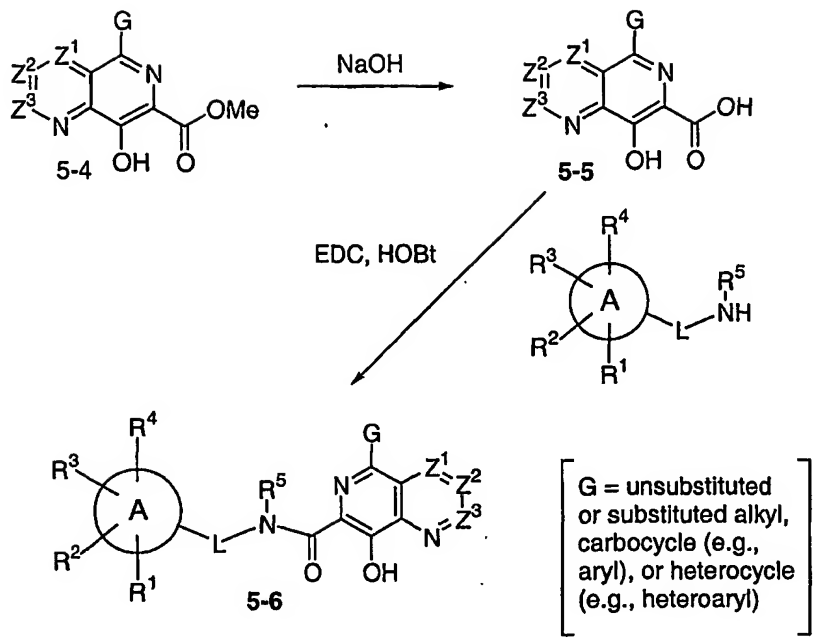




The preparation of compounds that feature additional substituents can be achieved as shown in Scheme 5. Oxidation of the alcohol **2-4** with manganese dioxide in an inert solvent such as methylene chloride will provide aldehyde **5-1**. The addition of Grignard reagents (such as phenyl magnesium bromide) to aldehyde moiety **5-1** can occur regioselectively to provide the alcohol **5-2**, which can then be elaborated to the compounds of the invention **5-6**.

SCHEME 5

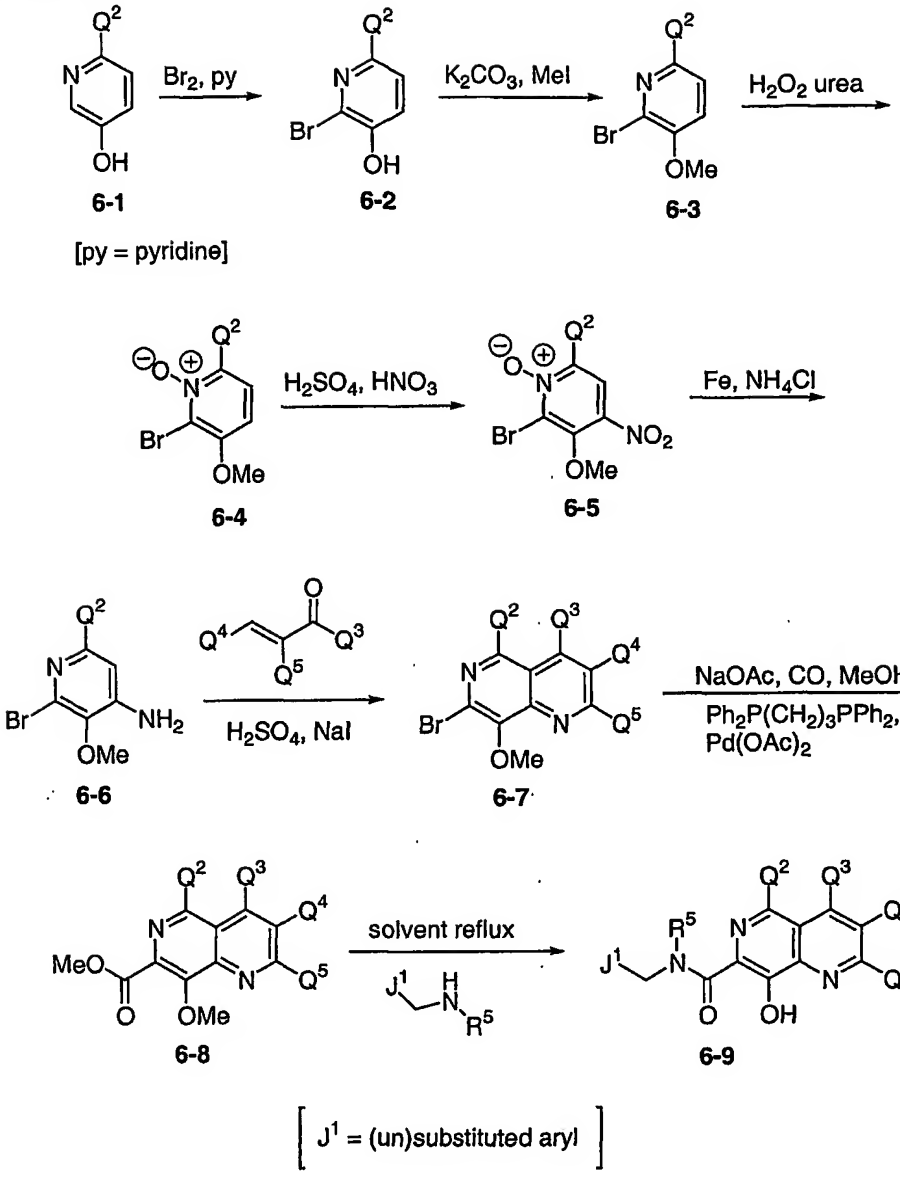




A further synthetic route to prepare compounds that are the subject of the invention is shown in Scheme 6. This methodology allows access to naphthyridine derivatives that are substituted at the 2, 3, 4 and 5 positions. Briefly, a 2-substituted 5-hydroxypyridine derivative **6-1** can be treated with bromine to undergo bromination at the 6 position to afford **6-2**, which can be converted to the methoxypyridine **6-3** and then oxidized to the corresponding N-oxide **6-4**. The N-oxide can be nitrated to provide **6-5**. Reduction of **6-5** with iron in the presence of ammonium chloride can provide the aniline **6-6**, which can be reacted with an alpha,beta-unsaturated aldehyde or ketone in the presence of an acid catalyst like sulfuric acid to provide **6-7** via an annulation. The bromide **6-7** can be elaborated to the amide **6-9** via a sequence of carbonylation and amidation reactions.

2-Substituted 5-hydroxypyridine derivatives of formula **6-1** can be prepared via methods described in Sorm et al., *Collect.Czech.Chem..Commun.*.1949, 14: 331,342; and Saksena et al., *Tetrahedron Lett.*1993, 34: 3267-3270: or routine variations thereof.

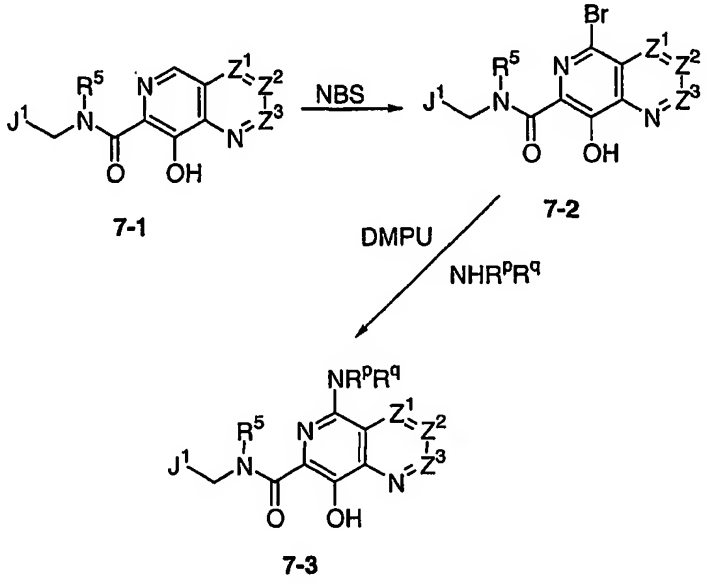
SCHEME 6



Compounds of the invention that comprise an amino substituent at the 5 position can be prepared in the manner set forth in Schemes 7 and 8. Bromination of the phenol **7-1** occurs regioselectively upon treatment with NBS in an inert solvent like methylene chloride to afford **7-2**. Reaction of this bromide with an amine at

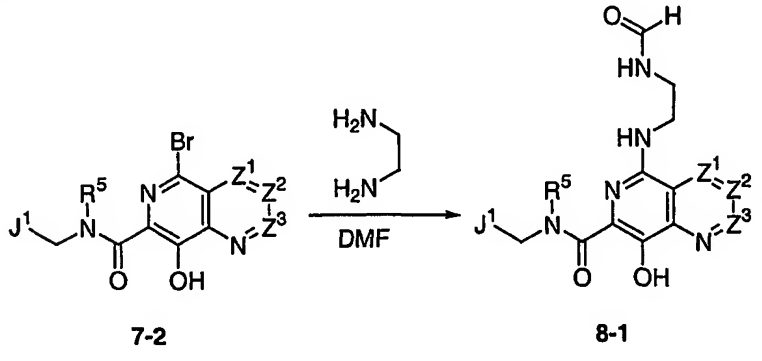
elevated temperatures in the presence of a polar solvent such as DMPU affords compounds of the invention **7-3**. Similar reaction of the bromide **7-2** (Scheme 8) with a diamine such as ethylene diamine in DMF as solvent will afford the formylated derivative **8-1** in addition to the expected diaminoethane derivative.

SCHEME 7



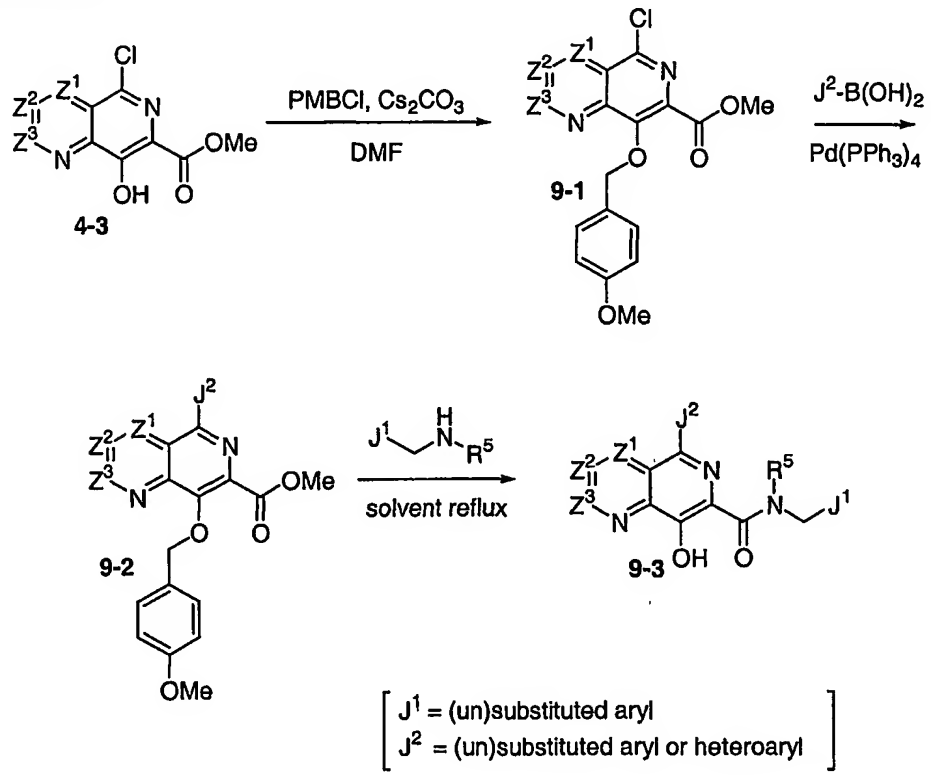
[J^1 = (un)substituted aryl
R^p, R^q = H; alkyl; alkyl substituted with, e.g., OH, alkoxy, carbocycle, or heterocycle; (un)substituted carbocycle, or (un)substituted heterocycle]

SCHEME 8



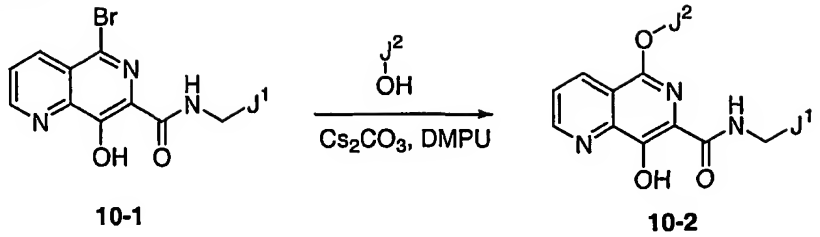
Preparation of aryl and heteroaryl derivatives via palladium cross coupling of the chloride **9-1** and the requisite boronic acids are depicted in Scheme 9.

SCHEME 9

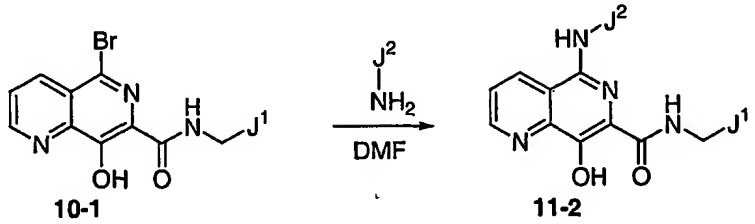


(Hetero)aryloxy, (hetero)arylamino, and (heteroaryl)thioxy derivatives **10-2**, **11-2**, and **12-2** respectively can be prepared as shown in Schemes 10 to 12, which exemplify the procedure for the naphthyridine core. The corresponding sulfone derivatives **12-2** can be obtained by oxidation of the sulfides **12-1** with either ozone or 3-chloroperbenzoic acid as shown in Scheme 12.

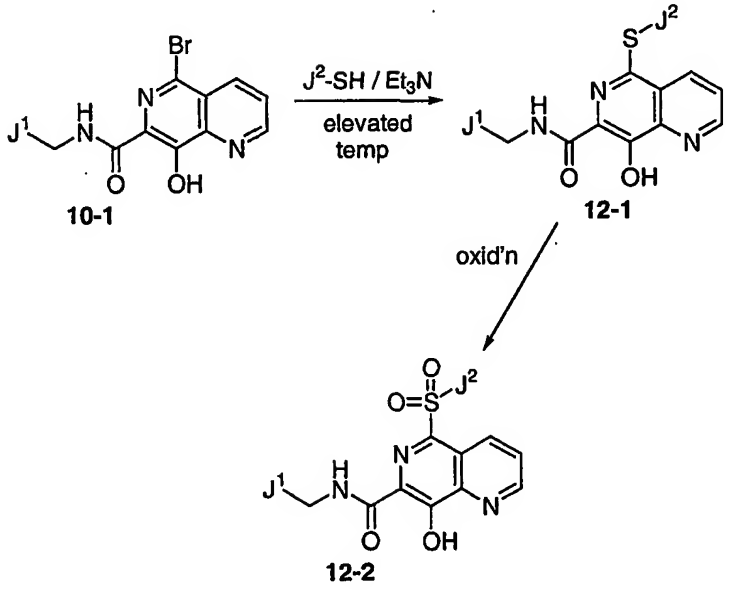
SCHEME 10



SCHEME 11



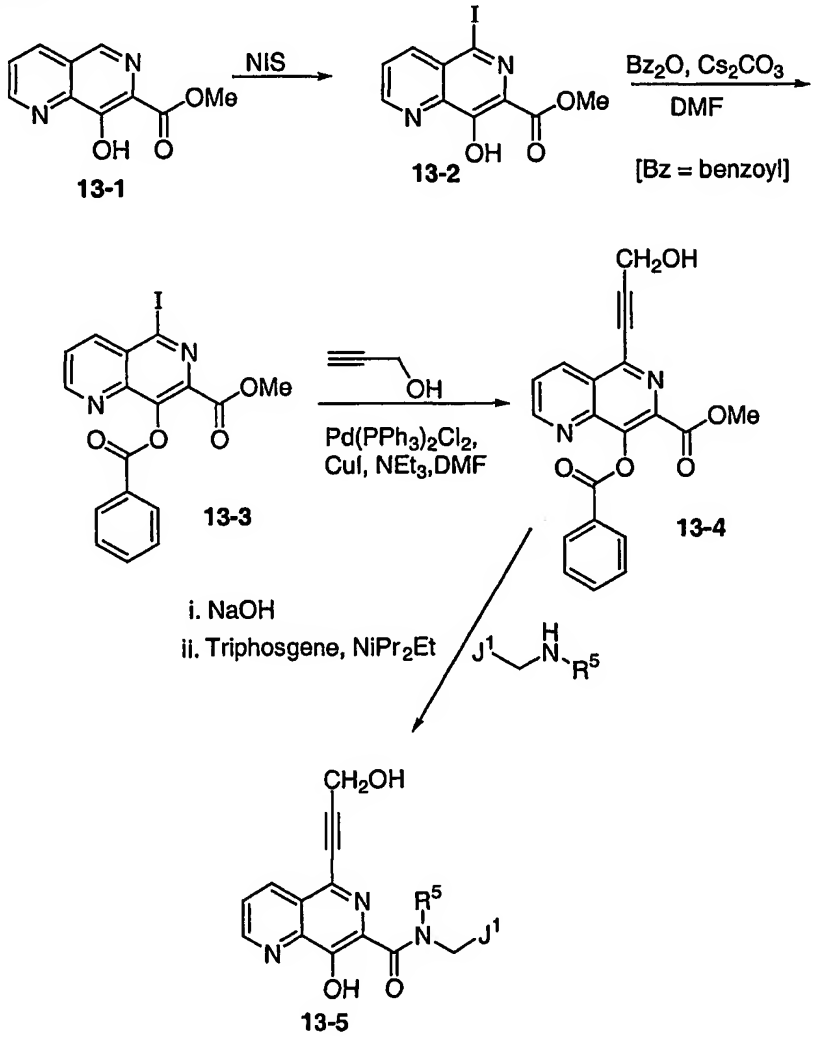
SCHEME 12



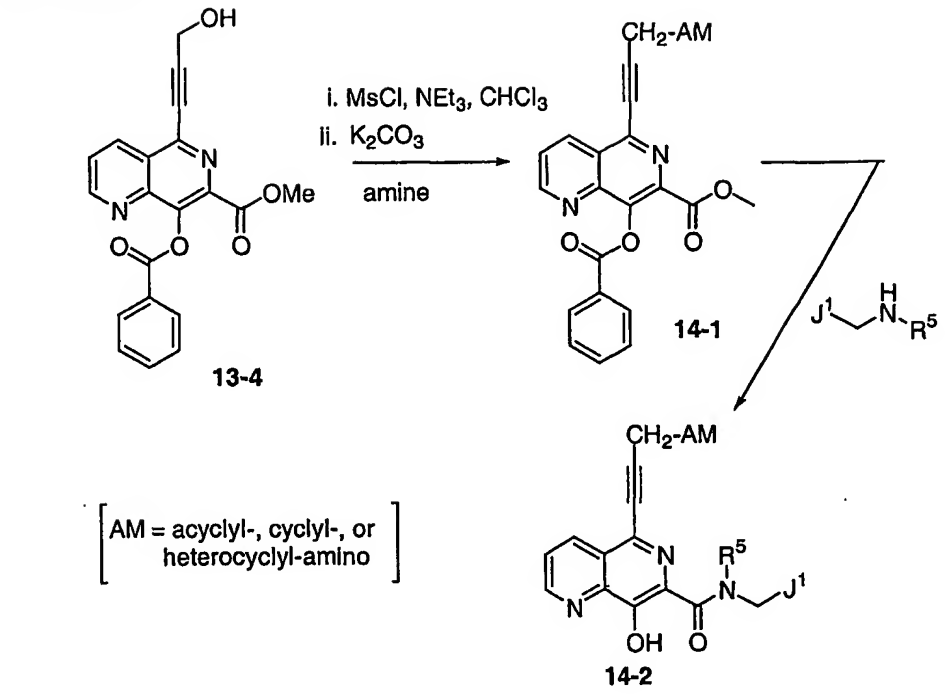
Preparation of compounds of the invention substituted with an acetylene can be prepared according to Scheme 13, which exemplifies the procedure for the naphthyridine core. Following protection of the iodide **13-2** as its benzoate **13-3**, the acetylenic group (for example propynol) can be appended by employing a

suitable palladium catalyst in the presence of copper iodide. Aminolysis of the ester **13-4** will afford the amide **13-5** with concomitant deprotection of the benzoate ester. Alternately the ester **13-4** can be converted to the corresponding amine and sulfone derivatives as shown in Schemes 14 and 15. Scheme 16 shows that the preparation of the nitrile derivative **16-2** can be achieved via a palladium catalyzed cyanation of the iodide **13-4**.

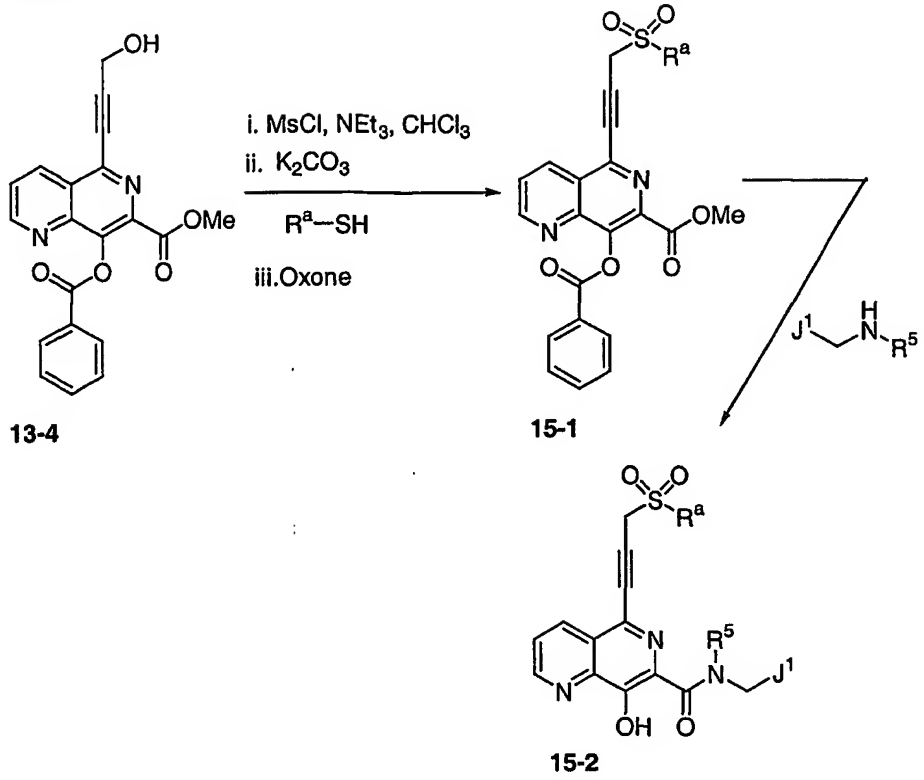
SCHEME 13



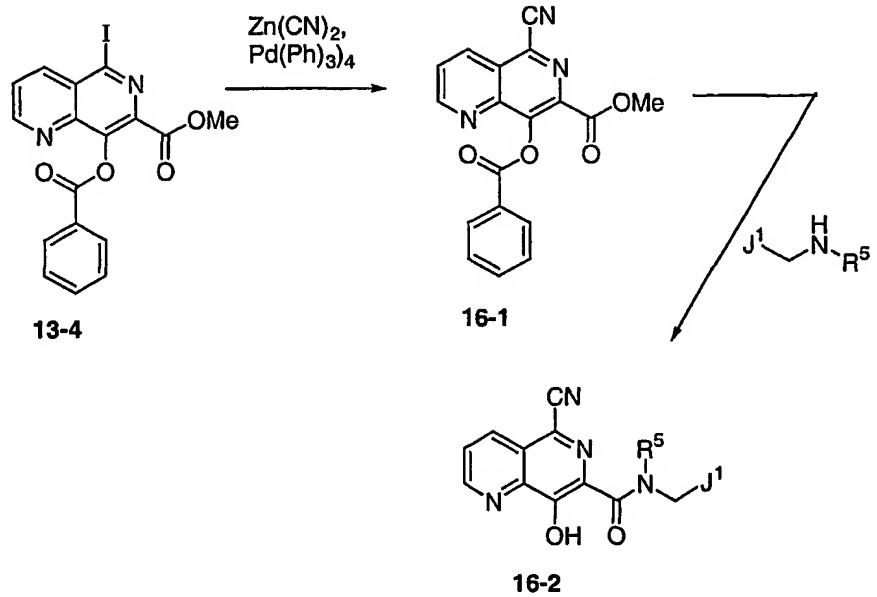
SCHEME 14


OH
OMe
i. MsCl, NEt3, CHCl3
ii. K2CO3
amine
CH2-AM
13-4
14-1
J1
H
N
R5
[AM = acyclyl-, cyclyl-, or heterocyclyl-amino]
14-2

SCHEME 15

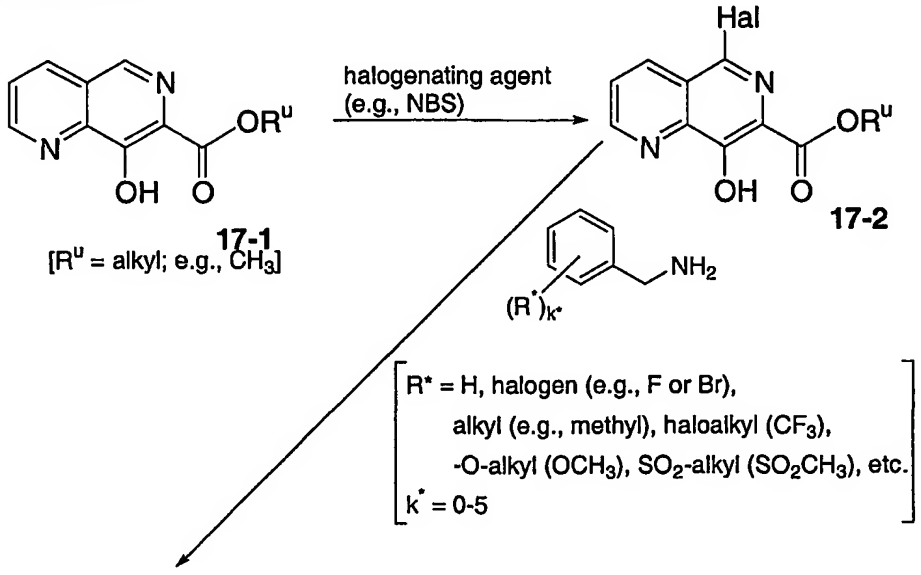


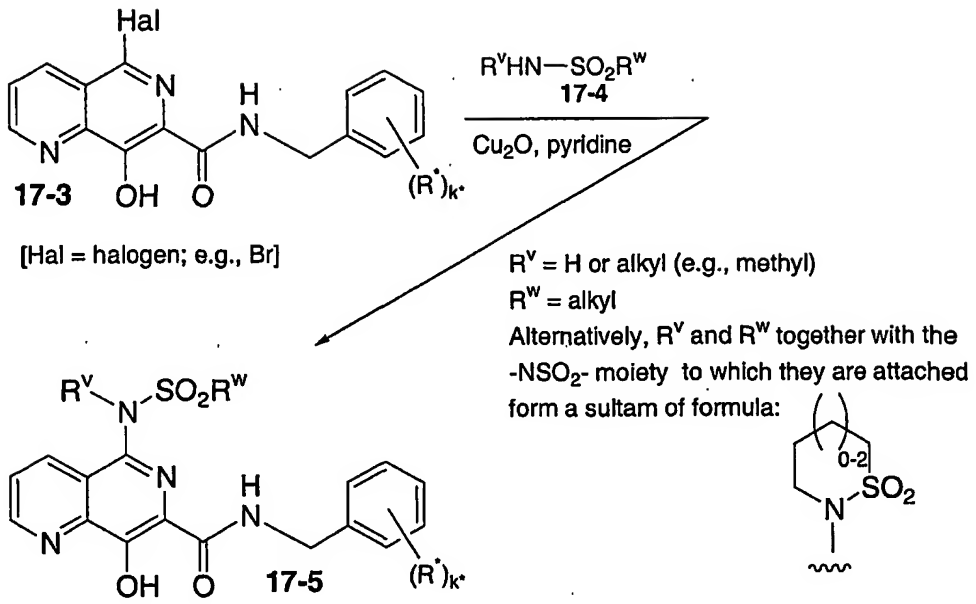
SCHEME 16



Preparation of compounds of the invention substituted with a sulfonamide can be prepared according to Scheme 17, which exemplifies the procedure for the naphthyridine core. The preparation includes halogenation of an alkyl 8-hydroxy-naphthyridine carboxylate (**17-1**) with a halogenation agent such as N-bromosuccinimide, coupling the halogenated ester (**17-2**) with substituted or unsubstituted benzylamine, and then condensing the 5-halo-8-hydroxy-naphthyridine carboxamide (**17-3**) with a sulfonamide (**17-4**) at elevated temperature (e.g., about 120 °C) in the presence of a copper promoter (e.g., copper(I) oxide) to afford the desired sulfonamidonaphthyridine product (**17-5**).

SCHEME 17



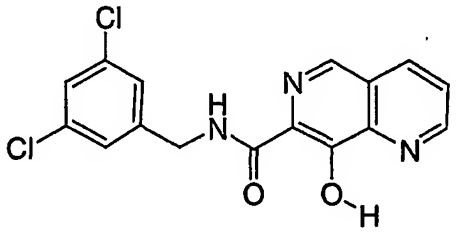


In the processes for preparing compounds of the present invention set forth in the foregoing schemes, functional groups in various moieties and substituents may be sensitive or reactive under the reaction conditions employed and/or in the presence of the reagents employed. Such sensitivity/reactivity can interfere with the progress of the desired reaction to reduce the yield of the desired product, or possibly even preclude its formation. Accordingly, it may be necessary or desirable to protect sensitive or reactive groups on any of the molecules concerned. Protection can be achieved by means of conventional protecting groups, such as those described in Protective Groups in Organic Chemistry, ed. J.F.W. McOmie, Plenum Press, 1973 and in T.W. Greene & P.G.M. Wuts, Protective Groups in Organic Synthesis, John Wiley & Sons, 1991. The protecting groups may be removed at a convenient subsequent stage using methods known in the art. Alternatively the interfering group can be introduced into the molecule subsequent to the reaction step of concern. For example, if one or more of the substituents R^1, R^2, R^3, and R^4 in compound **1-1** can interfere with the coupling reaction between compounds **1-1** and **1-2** of Scheme 1, the substituent can be incorporated into the molecule in a post-coupling step to afford Compound I.

The following examples serve only to illustrate the invention and its practice. The examples are not to be construed as limitations on the scope or spirit of the invention.

EXAMPLE 1

N-(3,5-dichlorobenzyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide



Step 1: Preparation of 3-{[Methoxycarbonylmethyl-(toluene-4-sulfonyl)-amino]-methyl}-pyridine-2-carboxylic acid isopropyl ester

Isopropyl 3-(hydroxymethyl)pyridine-2-carboxylate, (200 g, 1.02 mol; prepared as in P. Ornstein et. al. *J. Med. Chem.* 1989, 32, 827), methyl N-[(4-methylphenyl)sulfonyl]glycinate (249g, 1.02 mol), and triphenylphosphine (403g, 1.5 mol) were dissolved in dry THF (3000mls) and cooled to zero degrees under N2. The diethylazodicarboxylate (DEAD) (267.6 g, 1.5 mol) was dissolved in dry THF (250 mls) and placed in a 500 ml addition funnel. The DEAD was added dropwise over 1 hour. The ice bath was removed and the reaction was allowed to warm slowly to RT. After 2 hours, the reaction was checked by HPLC and some glycinate remained. More starting reagents were added and the reaction was left to stir at RT. After 30 min, the reaction was checked again and saw a very small amount of the glycinate remaining. Concentrated reaction down to a reddish-orange oil that was carried onto the next step.

Step 2: Preparation of methyl 8-hydroxy-1,6-naphthyridine-7-carboxylate

3-{[Methoxycarbonylmethyl-(toluene-4-sulfonyl)-amino]-methyl}-pyridine-2-carboxylic acid isopropyl ester (1.02 mol) was dissolved in dry methanol (4000ml) and cooled to zero degrees under nitrogen. Then via addition funnel, sodium methoxide (137.8g, 2.5 mol) was added slowly to avoid any exotherm. The reaction was stirred at zero degrees, and checked by HPLC after 1.5 hours and was found to be completed. The solvent was removed *in vacuo* to obtain a reddish-orange

oil, which was partitioned between water (1L) and ethyl acetate (1L). The organic layer was back extracted with saturated sodium bicarbonate solution. The pH of the aqueous layer was adjusted to 7, and the layer was maintained at this pH while extracting with methylene chloride. The organic layer was dried with Na2SO4, filtered, and the solvent was removed *in vacuo* to obtain a tan solid. The solid was dissolved in hot ethyl acetate, and the solution was filtered while hot to filter out any insoluble material. The product precipitated upon cooling. The precipitate was then filtered and dried in a vacuum oven. The filtrate was recrystallized by concentrating the filtrate and redissolving the resulting solid in a minimal amount of methylene chloride. Sufficient ethyl acetate was added to turn the solution slightly cloudy, after which the solution was boiled to reduce the volume, cooled, and the resulting crystals were filtered out and dried in a vacuum oven.

1H NMR (CDCl3, 500MHz) δ 11.794 (5H,s), 9.2 (1H,dd, *J*= 1.7 and 6.1Hz), 8.8 (1H,s), 8.3 (1H,dd, *J*= 1.5 and 9.7 Hz), 7.7 (1H, dd, *J*= 4.2 and 12.4 Hz), 4.1 (3H,s) ppm.

ES MS exact mass calculated for C10H8N2O3 204.1869 (MH+), found 205.1.

Step 3: Preparation of N-(3,5-dichlorobenzyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide

A slurry of the ester from step 2 (3.0g, 0.0147 mol) and 3,5,dichlorobenzylamine (2.85g, 0.016mol) in toluene (45 mL) were heated at reflux for 18hrs. Upon cooling to room temperature, the resulting solids were collected by filtration and washed 3 times with methanol (50ml; 30ml and 20ml)to afford the title compound as a white solid.

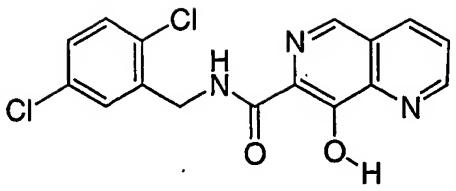
^{1}H NMR ($CDCl_3$, 400MHz) δ 13.1 (1H, s), 9.20 (1H, d, *J*=4.2 Hz), 8.68 (1H, s), 8.49 (1H, brs), 8.29 (1H, d, *J*=8.3Hz), 7.67 (1H, dd, *J*=8.3 and 4.2 Hz), 7.35-7.22 (3H, m), 4.67 (2H, d, *J*=5.4 Hz) ppm.

FAB MS calcd for $C_{16}H_{11}N_3O_2Cl_2$ 348 (MH^+), found 348.

FAB HRMS exact mass calcd for $C_{16}H_{11}N_3O_2Cl_2$ 348.0301 (MH^+), found 348.0294.

EXAMPLE 2

N-(2,5-dichlorobenzyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide



Step 1: Preparation of 8-hydroxy-1,6-naphthyridine-7-carboxylic acid

To a slurry of methyl 8-hydroxy-1,6-naphthyridine-7-carboxylate from Example 1 step 2 (1.50g, 7.35 mmol) in methanol (45ml) was added lithium hydroxide (22.0ml of a 1M aq. solution, 22.0 mmol) and the reaction was heated at 100°C for 7 hrs. Upon cooling to room temperature, hydrochloric acid (22.0ml of a 1M aq. solution, 22.0 mmol) was added and the reaction stirred for 16 hrs. The mixture was concentrated to a volume of 50 ml and neutralized with dilute $NaHCO_3$ (pH=7) The resulting precipitate was collected by filtration and washed with water and dried *in vacuo* to afford the title compound.

FAB MS calcd for $C_9H_6N_2O_3$ 191 (MH^+), found 191.

^1H NMR (d_6DMSO, 400MHz) δ 9.20 (1H, m), 8.72 (1H, s), 8.58 (1H, m), 7.80 (1H, dd, *J*=8.3 and 4.2 Hz) ppm.

Step 2: Preparation of N-(2,5-dichlorobenzyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide

Triphosgene (0.556g, 1.87 mmol) was added over 20 mins to a solution of the acid from step 1. (0.89g, 4.68 mmol) and diisopropylethylamine 3.26 ml, 18.7 mmol) in DMF (22 ml) at 0°C. The dark solution was allowed to warm to room temperature and stirred a further 1 hr. 2,5-dichlorobenzylamine (0.142 ml, 1.05 mmol) was treated with a portion of the above solution (0.58ml, 0.07 mmol) and the resulting mixture was stirred at room temperature for 16 hrs. The solution was treated with trifluroacetic acid (TFA) (0.025 ml) and purified by preparative HPLC. (Gilson semi preparative HPLC system and a YMC Combiprep Pro Column (50X20mm I.D., C18, S-5 um, 120A) (available from Waters) eluting with 5 - 95% acetonitrile/water (0.1% TFA) at 15 ml/min) to afford the title compound after lyophilization.

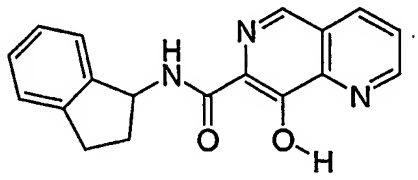
^1H NMR (d_6DMSO, 400MHz) δ 9.90 (1H, br t, *J*=5.0 Hz)), 9.20 (1H, d, *J*=4.0 Hz), 8.95 (1H, s), 8.65 (1H, d, *J*=8.0Hz), 7.85 (1H, dd, *J*=8.0 and 4.0 Hz), 7.54 (1H, d, *J*=8.0Hz), 7.50-7.30 (2H, m), 4.64 (2H, d, *J*=5.0 Hz) ppm.

FAB MS calcd for $C_{16}H_{11}N_3O_2Cl_2$ 348 (MH^+), found 348.

FAB HRMS exact mass calcd for $C_{16}H_{11}N_3O_2Cl_2$ 348.0301 (MH^+), found 348.0294.

EXAMPLE 3

N-[(1R,S)-2,3-dihydro-1H-inden-1-yl]-8-hydroxy-1,6-naphthyridine-7-carboxamide



The title compound was prepared using the procedure described in Example 2, Step 2 replacing 2,5 dichlorobenzylamine with 1(R,S) aminoindane.

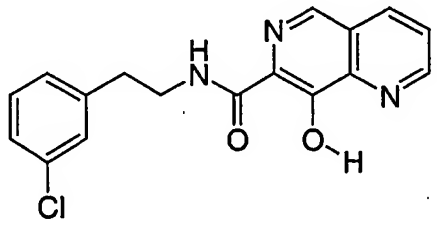
^1H NMR (d_6DMSO, 400MHz) δ 9.41 (1H, d, J=8.2Hz), 9.18 (1H, d, J=4.2 Hz), 8.90 (1H, s), 8.63 (1H, d, J=8.2Hz), 7.85 (1H, dd, J=8.2 and 4.2 Hz), 7.35-7.10 (4H, m), 5.63 (1H, q, J=8.2 Hz), 3.20-2.80 (2H, m), 2.60-2.40 (1H, m), 2.30-2.10 (1H, m) ppm.

FAB MS calcd for $C_{18}H_{15}N_3O_2$ 306 (MH^+), found 306.

FAB HRMS exact mass calcd for $C_{18}H_{15}N_3O_2$ 306.1237 (MH^+), found 306.1230

EXAMPLE 4

N-[2-(3-chlorophenyl)ethyl]-8-hydroxy-1,6-naphthyridine-7-carboxamide



The title compound was prepared using the procedure described in Example 2, Step 2 replacing 2,5 dichlorobenzylamine with 3 chlorophenethylamine.

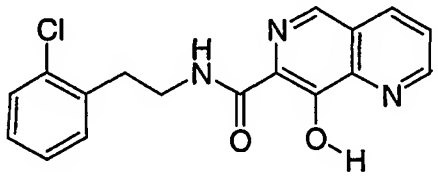
^1H NMR (d_6DMSO, 400MHz) δ 9.39 (1H, m), 9.17 (1H, d, J=4.2 Hz), 8.91 (1H, s), 8.61 (1H, d, J=8.3Hz), 7.84 (1H, dd, J=8.3 and 4.2 Hz), 7.40-7.20 (4H, m), 3.63 (2H, m), 2.96 (2H, t, J=7.2Hz) ppm.

FAB MS calcd for $C_{17}H_{14}N_3O_2Cl$ 328 (MH^+), found 328.

FAB HRMS exact mass calcd for $C_{17}H_{14}N_3O_2Cl$ 328.0847 (MH^+), found 328.0841.

EXAMPLE 5

N-[2-(2-chlorophenyl)ethyl]-8-hydroxy-1,6-naphthyridine-7-carboxamide



The title compound was prepared using the procedure described in Example 2, Step 2 replacing 2,5 dichlorobenzylamine with 2 chlorophenethylamine.

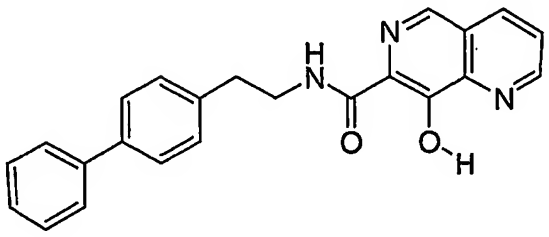
^1H NMR (d_6DMSO, 400MHz) δ 9.45 (1H, m), 9.17 (1H, d, *J*=4.2 Hz), 8.91 (1H, s), 8.61 (1H, d, *J*=8.3Hz), 7.84 (1H, dd, *J*=8.3 and 4.2 Hz), 7.60-7.20 (4H, m), 3.65 (2H, m), 3.07 (2H, t, *J*=7.2Hz) ppm.

FAB MS calcd for $C_{17}H_{14}N_3O_2Cl$ 328 (MH^+), found 328.

FAB HRMS exact mass calcd for $C_{17}H_{14}N_3O_2Cl$ 328.0847 (MH^+), found 328.0842.

EXAMPLE 6

N-[2-(1,1'-biphenyl-4-yl)ethyl]-8-hydroxy-1,6-naphthyridine-7-carboxamide



The title compound was prepared using the procedure described in Example 2, Step 2 replacing 2,5 dichlorobenzylamine with 4 phenylphenethylamine.

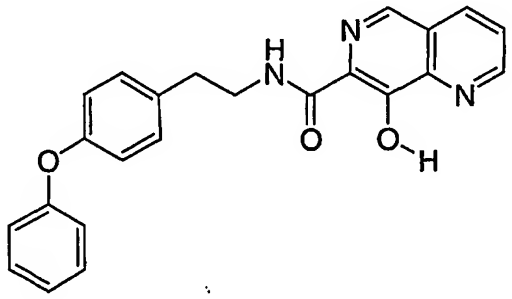
^1H NMR (d_6DMSO, 400MHz) δ 9.41 (1H, m), 9.17 (1H, d, *J*=4.2 Hz), 8.91 (1H, s), 8.61 (1H, d, *J*=8.2Hz), 7.84 (1H, dd, *J*=8.2 and 4.2 Hz), 7.64 (2H, d, *J*=7.4Hz), 7.61(2H, d, *J*=8.0Hz), 7.45(2H, d, *J*=7.6Hz), 7.40-7.30 (3H, m), 3.65 (2H, m), 2.99 (2H, t, *J*=7.3Hz) ppm.

FAB MS calcd for $C_{23}H_{19}N_3O_2$ 370 (MH^+), found 370.

FAB HRMS exact mass calcd for $C_{23}H_{19}N_3O_2$ 370.1550 (MH^+), found 370.1554.

EXAMPLE 7

8-hydroxy-N-[2-(4-phenoxyphenyl)ethyl]-1,6-naphthyridine-7-carboxamide



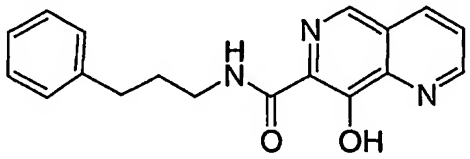
The title compound was prepared using the procedure described in Example 2, Step 2 replacing 2,5 dichlorobenzylamine with 4 phenoxyphenethylamine. ^1H NMR (d_6DMSO, 400MHz) δ 9.38 (1H, m), 9.17 (1H, d, *J*=4.2 Hz), 8.91 (1H, s), 8.61 (1H, d, *J*=8.3Hz), 7.84 (1H, dd, *J*=8.3 and 4.2 Hz), 7.36 (2H, t, *J*=7.5Hz), 7.29 (2H, d, *J*=8.2Hz), 7.10 (1H, dt, *J*=7.4 and 1.0Hz), 7.00-6.90 (4H, m), 3.61 (2H, m), 2.92 (2H, t, *J*=7.4Hz) ppm.

FAB MS calcd for $C_{23}H_{19}N_3O_3$ 386 (MH^+), found 386.

FAB HRMS exact mass calcd for $C_{23}H_{19}N_3O_3$ 386.1499 (MH^+), found 386.1495.

EXAMPLE 8

8-hydroxy-N-(3-phenylpropyl)-1,6-naphthyridine-7-carboxamide

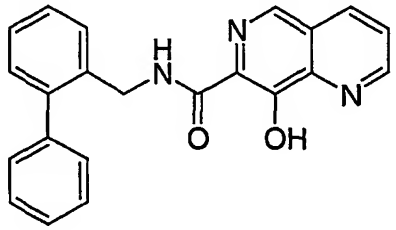


The title compound was prepared using the procedure described in Example 2, Step 2 replacing 2,5 dichlorobenzylamine with 3-phenylproplyamine. ^1H NMR (DMSO-d6, 400MHz) δ 9.38 (1H, t, *J*=5.5Hz), 9.16 (1H, d, *J*=4.2Hz), 8.91 (1H, s), 8.61 (1H, d, *J*=8.2Hz), 7.83 (1H, dd, *J*=4.2 and 8.2Hz), 7.25 (4H, m), 7.17 (1H, t, 7Hz), 3.41 (2H, m), 2.65 (2H, t, *J*=7.5Hz) and 1.92 (2H, quintet, *J*=7.3Hz)ppm.

FAB MS calcd for $C_{18}H_{17}N_3O_2$ 308.1 (MH^+), found 308.1.
FAB HRMS exact mass calcd for $C_{18}H_{17}N_3O_2$ 308.1394 (MH^+), found 308.1379.

EXAMPLE 9

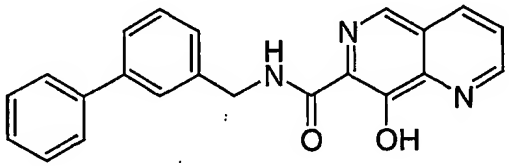
N-(1,1'-biphenyl-2-ylmethyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide



The title compound was prepared using the procedure described in Example 2, Step 2 replacing 2,5 dichlorobenzylamine with 2-phenylbenzylamine.
^{1}H NMR (DMSO-d6, 400MHz) δ 9.68 (1H, br s), 9.16 (1H, d, *J*=4.2Hz), 8.91 (1H, s), 8.61 (1H, d, *J*=8.4Hz), 7.83 (1H, dd, *J*=4.2 and 8.2Hz), 7.31-7.51 (8H, m), 7.24 (1H, m) and 4.54 (2H, m)ppm.
FAB MS calcd for $C_{22}H_{17}N_3O_2$ 356.1 (MH^+), found 356.1.
FAB HRMS exact mass calcd for $C_{22}H_{17}N_3O_2$ 356.1394 (MH^+), found 356.1416.

EXAMPLE 10

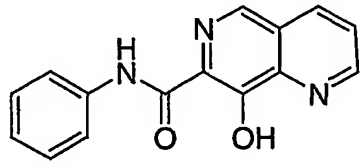
N-(1,1'-biphenyl-3-ylmethyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide



The title compound was prepared using the procedure described in Example 2, Step 2 replacing 2,5 dichlorobenzylamine with 3-phenylbenzylamine.
^{1}H NMR (DMSO-d6, 400MHz) • 9.93 (1H, br s), 9.16 (1H, d, *J*=4.4Hz), 8.93 (1H, s), 8.62 (1H, d, *J*=8.2Hz), 7.83 (1H, dd, *J*=4.2 and 8.2Hz), 7.70 (1H, s), 7.64 (2H, d, 8.4Hz), 7.56 (1H, d, 7.3Hz), 7.33-7.51 (5H, m) and 4.64 (2H, m)ppm.
FAB MS calcd for $C_{22}H_{17}N_3O_2$ 356.1 (MH^+), found 356.1.
FAB HRMS exact mass calcd for $C_{22}H_{17}N_3O_2$ 356.1394 (MH^+), found 356.1410.

EXAMPLE 11

8-hydroxy-N-phenyl-1,6-naphthyridine-7-carboxamide



The title compound was prepared using the procedure described in Example 2, Step 2 replacing 2,5 dichlorobenzylamine with aniline.

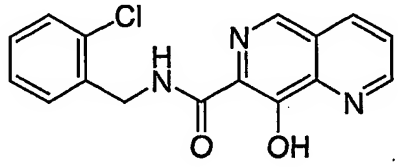
^{1}H NMR (DMSO-d6, 400MHz) δ 11.0 (1H, br s), 9.19 (1H, br s), 9.00 (1H, br s), 8.65 (1H, d, *J*=8.0Hz), 7.88 (3H, m), 7.41 (2H, t, *J*=7.7Hz), 7.19 (1H, t, *J*=7.0)ppm.

FAB MS calcd for $C_{15}H_{11}N_3O_2$ 266.1 (MH^+), found 266.1.

FAB HRMS exact mass calcd for $C_{15}H_{11}N_3O_2$ 266.0924 (MH^+), found 266.0926.

EXAMPLE 12

8 N-(2-chlorobenzyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide



The title compound was prepared using the procedure described in Example 2, Step 2 replacing 2,5 dichlorobenzylamine with 2-chlorobenzylamine.

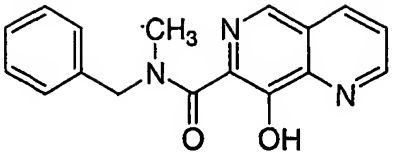
^{1}H NMR (DMSO-d6, 400MHz) δ 9.84 (1H, br s), 9.18 (1H, d, *J*=4.3Hz), 8.96 (1H, s), 8.64 (1H, d, *J*=8.3Hz), 7.85 (1H, dd, *J*=8.3 and 4.3Hz), 7.48 (1H, m), 7.38 (1H, m), 7.33 (2H, m), 4.65 (2H, m)ppm.

FAB MS calcd for $C_{16}H_{12}ClN_3O_2$ 314.1 (MH^+), found 314.1.

FAB HRMS exact mass calcd for $C_{16}H_{12}ClN_3O_2$ 314.0691 (MH^+), found 314.0702.

EXAMPLE 13

N-benzyl-8-hydroxy-N-methyl-1,6-naphthyridine-7-carboxamide



The title compound was prepared using the procedure described in Example 2, Step 2 replacing 2,5 dichlorobenzylamine with N-methylbenzylamine.

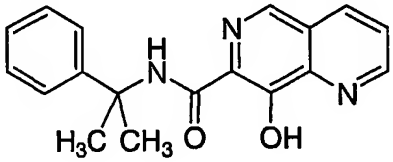
^{1}H NMR (DMSO-d6, 400MHz) δ 9.14 (1H, m), 8.91 (1H, 2s), 8.60 (1H, 2d, *J*=8.4Hz), 7.78 (1H, m), 7.32-7.44 (5H, m), 4.76 (1.15H, s), 4.46 (0.85H, s), 2.91 (1.7h, s) and 2.79 (1.3H, s)ppm.

FAB MS calcd for $C_{17}H_{15}N_3O_2$ 294.1 (MH^+), found 294.1.

FAB HRMS exact mass calcd for $C_{17}H_{15}N_3O_2$ 294.1237 (MH^+), found 294.1244.

EXAMPLE 14

8-hydroxy-N-(1-methyl-1-phenylethyl)-1,6-naphthyridine-7-carboxamide



The title compound was prepared using the procedure described in Example 2, Step 2 replacing 2,5 dichlorobenzylamine with cumylamine.

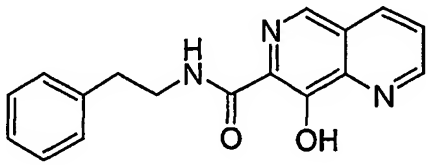
^{1}H NMR (DMSO-d6, 400MHz) δ .16 (1H, br s), 8.94 (1H, s), 8.62 (1H, d, *J*=8.2Hz), 7.83 (1H, m), 7.46 (2H, d, *J*=7.1Hz), 7.34 (2H, t, *J*=7.6Hz), 7.23 (1H, m) and 1.80 (6H, s)ppm.

FAB MS calcd for $C_{18}H_{17}N_3O_2$ 308.1 (MH^+), found 308.1.

FAB HRMS exact mass calcd for $C_{18}H_{17}N_3O_2$ 308.1394 (MH^+), found 308.1378.

EXAMPLE 15

8-hydroxy-N-(2-phenylethyl)-1,6-naphthyridine-7-carboxamide



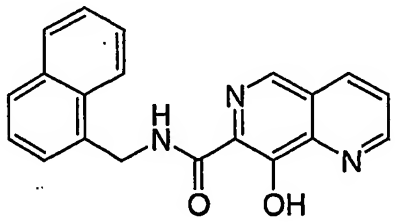
The title compound was prepared using the procedure described in Example 2, Step 2 replacing 2,5 dichlorobenzylamine with phenethylamine.

^{1}H NMR (DMSO-d6, 400MHz) δ 9.36 (1H, br s), 9.16 (1H, d, *J*=4.2Hz), 8.90 (1H, s), 8.61 (1H, d, *J*=8.2Hz), 7.83 (1H, dd, *J*=4.2 and 8.2Hz), 7.25-7.36 (4H, m), 7.21(1H, m), 3.61(2H, m) and 2.94 (2H, t, 7.5Hz)ppm.

FAB MS calcd for $C_{17}H_{15}N_3O_2$ 294.1 (MH^+), found 294.1.

EXAMPLE 16

8-hydroxy-N-(1-naphthylmethyl)-1,6-naphthyridine-7-carboxamide



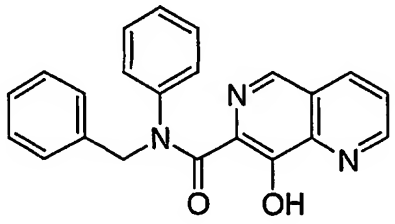
The title compound was prepared using the procedure described in Example 2, Step 2 replacing 2,5 dichlorobenzylamine with 1-naphthalenemethylamine.

^{1}H NMR (DMSO-d6, 400MHz) δ 9.86 (1H, br s), 9.17 (1H, d, *J*=3.7Hz), 8.92 (1H, s), 8.62 (1H, d, *J*=8.2Hz), 8.31 (1H, d, *J*=8.2Hz), 7.97 (1H, d, *J*=7.7Hz), 7.87 (1H, d, *J*=8.2Hz), 7.84 (1H, dd, *J*=4.2 and 8.2Hz), 7.61 (1H, m), 7.56 (2H, m), 7.49 (1H, t, *J*=7.7Hz), and 5.05 (2H, d, *J*=4.2Hz)ppm.

FAB MS calcd for $C_{20}H_{15}N_3O_2$ 330.1 (MH^+), found 330.1.

EXAMPLE 17

N-benzyl-8-hydroxy-N-phenyl-1,6-naphthyridine-7-carboxamide

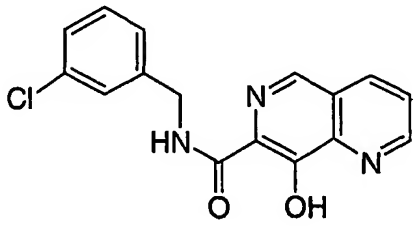


The title compound was prepared using the procedure described in Example 2, Step 2 replacing 2,5 dichlorobenzylamine with N-phenylbenzylamine.

^{1}H NMR (d_6DMSO, 400MHz) δ 10.79 (1H, m), 9.04 (1H, s), 8.69 (1H, m), 8.46 (1H, m), 7.68 (1H, m), 7.50-6.90 (7H, m), 6.70-6.40 (3H, m), 5.14 (2H, m) ppm.
FAB MS calcd for $C_{22}H_{17}N_3O_2$ 386 (MH^+), found 356.
FAB HRMS exact mass calcd for $C_{22}H_{17}N_3O_2$ 356.13935 (MH^+), found 356.13689.

EXAMPLE 18

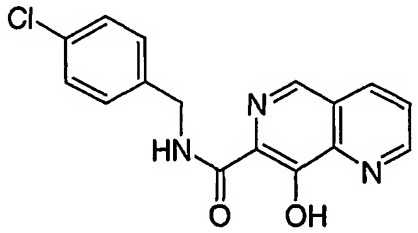
N-(3-chlorobenzyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide



The title compound was prepared using the procedure described in Example 2, Step 2 replacing 2,5 dichlorobenzylamine with 3-chlorobenzylamine.
^{1}H NMR (d_6DMSO, 400MHz) δ 9.94(1H, br t, *J*=5.6 Hz)), 9.17 (1H, d, *J*=4.2 Hz), 8.93 (1H, s), 8.63 (1H, d, *J*=8.3Hz), 7.85 (1H, dd, *J*=8.3 and 4.2 Hz), 7.45(1H, s), 7.50-7.30 (3H, m), 4.58 (2H, d, *J*=6.0 Hz) ppm.
FAB MS calcd for $C_{16}H_{12}ClN_3O_2$ 314 (MH^+), found 314.

EXAMPLE 19

N-(4-chlorobenzyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide



The title compound was prepared using the procedure described in Example 2, Step 2 replacing 2,5 dichlorobenzylamine with 4-chlorobenzylamine.

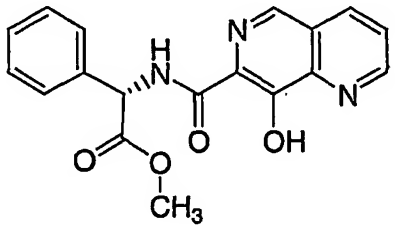
^{1}H NMR (d_6DMSO, 400MHz) δ 9.92 (1H, br t, *J*=5.0 Hz), 9.17 (1H, d, *J*=4.3 Hz), 8.93 (1H, s), 8.63 (1H, d, *J*=8.3Hz), 7.85 (1H, ddd, *J*=8.3, 4.2 and 1.5 Hz), 7.41(4H, s), 4.58 (2H, d, *J*=6.3 Hz) ppm.

FAB MS calcd for $C_{16}H_{12}ClN_3O_2$ 314 (MH^+), found 314.

FAB HRMS exact mass calcd for $C_{16}H_{12}ClN_3O_2$ 314.0691 (MH^+), found 314.06908.

EXAMPLE 20

Methyl (2S)-{[(8-hydroxy-1,6-naphthyridin-7-yl)carbonyl]amino} (phenyl)ethanoate



The title compound was prepared using the procedure described in Example 2, Step 2 replacing 2,5 dichlorobenzylamine with S(+)-2-phenylglycine methyl ester..

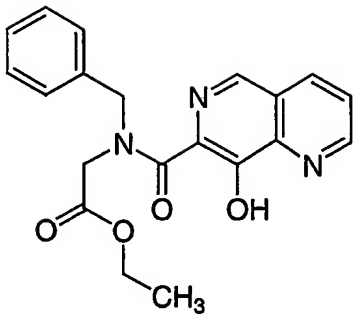
^{1}H NMR (d_6DMSO, 400MHz) δ 9.82 (1H, m), 9.17 (1H, d, *J*=4.2 Hz), 8.94 (1H, s), 8.64 (1H, d, *J*=8.2Hz), 7.85 (1H, ddd, *J*=8.2, 4.2 and 1.5 Hz), 7.60-7.30 (5H, m), 5.82 (1H, d, *J*=7.5 Hz), 3.72 (3H, s) ppm.

FAB MS calcd for $C_{18}H_{15}N_3O_4$ 338(MH^+), found 338.

FAB HRMS exact mass calcd for $C_{18}H_{15}N_3O_4$ 338.11353 (MH^+), found 338.11418.

EXAMPLE 21

Ethyl N-benzyl-N-[(8-hydroxy-1,6-naphthyridin-7-yl)carbonyl]glycinate



The title compound was prepared using the procedure described in Example 2, Step 2 replacing 2,5 dichlorobenzylamine with N-benzylglycine ethyl ester..

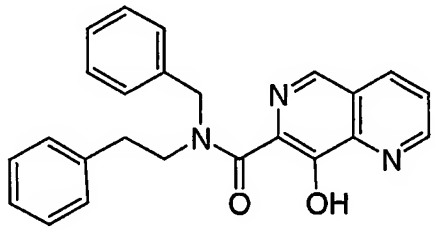
^{1}H NMR (d_6DMSO, 400MHz) δ 9.15 (1H, m), 8.90 (0.5H, s), 8.85 (0.5H, s), 8.59 (1H, m), 7.80 (1H, m), 7.50-7.20 (5H, m), 4.85 (1H, s), 4.60 (1H, s), 4.23 (1H, s), 4.20-4.09 (2H, m), 4.02 (1H, q, *J*=7.0Hz), 1.21 (1H, t, *J*=7.0Hz), 1.08 (1H, t, *J*=7.0Hz) ppm.

FAB MS calcd for $C_{18}H_{15}N_3O_4$ 366 (MH^+), found 366.

FAB HRMS exact mass calcd for $C_{18}H_{15}N_3O_4$ 366.144833 (MH^+), found 366.144987.

EXAMPLE 22

N-benzyl-8-hydroxy-N-(2-phenylethyl)-1,6-naphthyridine-7-carboxamide



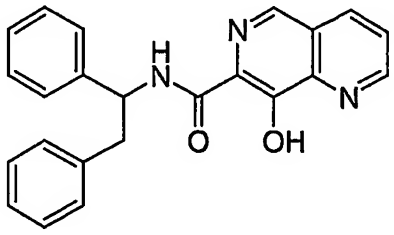
The title compound was prepared using the procedure described in Example 2, Step 2 replacing 2,5 dichlorobenzylamine with N-benzyl-2-phenethylamine..

^{1}H NMR (d_6DMSO, 400MHz) δ 9.25-9.15 (1H, m), 8.99 (0.6H, s), 8.92 (0.4H, s), 8.64 (0.6H, d, *J*=8.3Hz), 8.59 (0.4H, d, *J*=8.3Hz), 7.90-7.75 (1H, m), 7.50-7.00(10H, m), 6.85 (1H, d, *J*=7.3Hz), 4.77 (1.2H, s), 4.41 (0.8H, s), 3.52 (0.8H, t, *J*=8.0Hz), 3.34 (1.2H, t, *J*=8.0Hz), 2.86 (0.8H, t, *J*=8.0Hz), 2.79 (1.2H, t, *J*=8.0Hz) ppm.

FAB MS calcd for $C_{24}H_{21}N_3O_2$ 384 (MH^+), found 384.
FAB HRMS exact mass calcd for $C_{24}H_{21}N_3O_2$ 384.17074 (MH^+), found 384.17065.

EXAMPLE 23

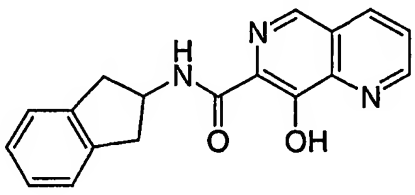
N-(1,2-diphenylethyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide



The title compound was prepared using the procedure described in Example 2, Step 2 replacing 2,5 dichlorobenzylamine with 1,2-diphenethylamine..
^1H NMR (d_6DMSO, 400MHz) δ 9.77 (1H, d, J=9.0 Hz), 9.14 (1H, d, J=4.2 Hz), 8.93 (1H, s), 8.60 (1H, d, J=8.3Hz), 7.85 (1H, ddd, J=8.3, 4.2 and 0.8 Hz), 7.56 (2H, d, J=7.7Hz), 7.40-7.00 (8H, m), 5.37 (1H,m), 3.44 (1H, dd, J=10 and 13.6 Hz), 3.16 (1H, dd, J=10 and 5.4 Hz) ppm.
FAB MS calcd for $C_{23}H_{19}N_3O_2$ 370 (MH^+), found 370.
FAB HRMS exact mass calcd for $C_{23}H_{19}N_3O_2$ 370.155003 (MH^+), found 370.155737.

EXAMPLE 24

N-(2,3-dihydro-1H-inden-2-yl)-8-hydroxy-1,6-naphthyridine-7-carboxamide



The title compound was prepared using the procedure described in Example 2, Step 2 replacing 2,5 dichlorobenzylamine with 2-aminoindane hydrochloride.

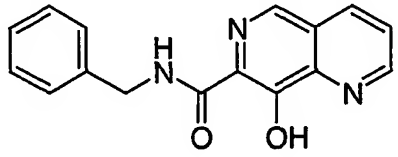
^{1}H NMR (d_6DMSO, 400MHz) δ 9.64 (1H, d, *J*=7.8 Hz), 9.17 (1H, d, *J*=3.6 Hz), 8.90 (1H, s), 8.61 (1H, d, *J*=8.3Hz), 7.84 (1H, ddd, *J*=8.3, 4.2 and 1.0 Hz), 7.30-7.10 (4H, m), 4.83 (1H, q, *J*=7.7), 3.25 (2H, dd, *J*=7.6 and 13.6 Hz), 3.14 (2H, dd, *J*=7.6 and 15.6 Hz) ppm.

FAB MS calcd for $C_{18}H_{15}N_3O_2$ 306 (MH^+), found 306.

FAB HRMS exact mass calcd for $C_{18}H_{15}N_3O_2$ 306.123703 (MH^+), found 306.122288.

EXAMPLE 25

N-benzyl-8-hydroxy-1,6-naphthyridine-7-carboxamide



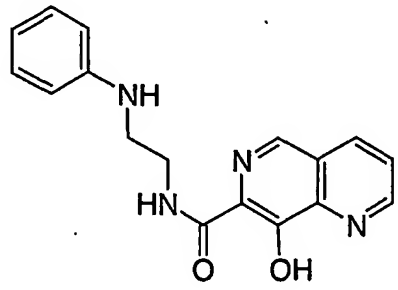
The title compound was prepared using the procedure described in Example 2, Step 2 replacing 2,5 dichlorobenzylamine with benzylamine.

^{1}H NMR (CD3OD, 400MHz) δ 9.13 (1H, d, *J*=4.3Hz), 8.88 (1H, s), 8.66 (1H, d, *J*=8.3Hz), 7.87 (1H, dd, *J*=4.5 and 8.4Hz), 7.43 (2H, d, *J*=9.7Hz), 7.33 (2H, m), 7.26 (1H, m), and 4.67 (2H, s)ppm.

FAB MS calcd for $C_{16}H_{13}N_3O_2$ 280.1 (MH^+), found 280.0.

EXAMPLE 26

N-(2-anilinoethyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide



The title compound was prepared using the procedure described in Example 2, Step 2 replacing 2,5 dichlorobenzylamine with N-phenethyldiamine.

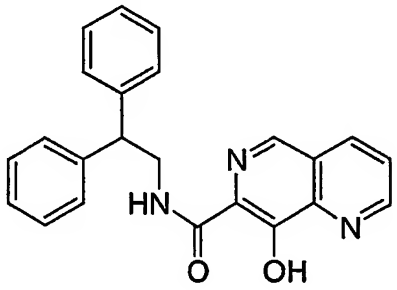
^{1}H NMR (d_6DMSO, 400MHz) δ 9.44 (1H, t, *J*=5.7 Hz), 9.17 (1H, d, *J*=4.2 Hz), 8.92 (1H, s), 8.62 (1H, d, *J*=8.2Hz), 7.84 (1H, dd, *J*=8.3 and 4.2 Hz), 7.10 (2H, t, *J*=8.2Hz), 6.68 (2H,d, *J*=8.2Hz), 6.58 (1H,t, *J*=7.1Hz), 3.57 (2H, q, *J*=6.0Hz), 3.29 (2H, t, *J*=7.6Hz) ppm.

FAB MS calcd for $C_{17}H_{16}N_4O_2$ 309 (MH^+), found 309.

FAB HRMS exact mass calcd for $C_{17}H_{16}N_4O_2$ 309.1346022 (MH^+), found 309.133004.

EXAMPLE 27

N-(2,2-diphenylethyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide



The title compound was prepared using the procedure described in Example 2, Step 2 replacing 2,5 dichlorobenzylamine with 2,2-diphenylethylamine.

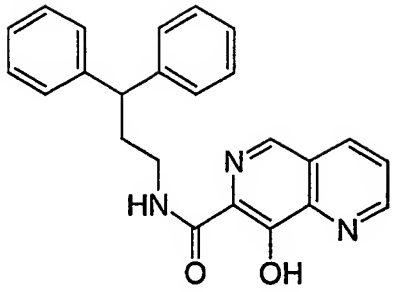
^{1}H NMR (d_6DMSO, 400MHz) δ 9.21 (1H, t, *J*=5.7 Hz), 9.14 (1H, d, *J*=4.3 Hz), 8.82 (1H, s), 8.57 (1H, d, *J*=8.4Hz), 7.81 (1H, dd, *J*=8.4 and 4.3 Hz), 7.38(4H, d, *J*=7.6Hz), 7.30 (4H,d, *J*=7.6Hz), 7.19 (2H, t, *J*=7.7Hz), 4.58 (2H, t, *J*=7.0Hz), 4.05 (2H, t, *J*=7.0Hz) ppm.

FAB MS calcd for $C_{23}H_{19}N_3O_2$ 370 (MH^+), found 370.

FAB HRMS exact mass calcd for $C_{23}H_{19}N_3O_2$ 370.155033 (MH^+), found 370.1556930.

EXAMPLE 28

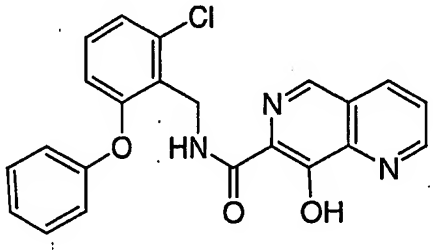
N-(3,3-diphenylpropyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide



The title compound was prepared using the procedure described in Example 2, Step 2 replacing 2,5 dichlorobenzylamine with 3,3-diphenylpropylamine.
^{1}H NMR (d_6DMSO, 400MHz) δ 9.36 (1H, t, *J*=5.7 Hz), 9.14 (1H, d, *J*=4.3 Hz), 8.89 (1H, s), 8.61 (1H, d, *J*=8.3Hz), 7.82 (1H, dd, *J*=8.3 and 4.3 Hz), 7.35 (4H, d, *J*=7.6Hz), 7.29 (4H, d, *J*=7.6Hz), 7.16 (2H, t, *J*=7.7Hz), 4.05 (2H, t, *J*=7.9Hz), 3.31 (2H, m) and 2.40 (2H, q, *J*=7.5Hz) ppm.
FAB MS calcd for $C_{24}H_{21}N_3O_2$ 384 (MH^+), found 384.
FAB HRMS exact mass calcd for $C_{24}H_{21}N_3O_2$ 384.1707 (MH^+), found 384.1708

EXAMPLE 29

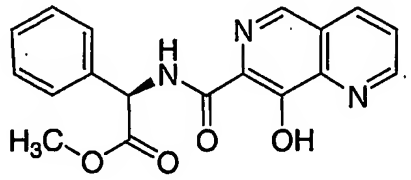
N-(2-chloro-6-phenoxybenzyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide



The title compound was prepared using the procedure described in Example 2, Step 2 replacing 2,5 dichlorobenzylamine with 2-aminomethyl-3-chlorodiphenylether.
^{1}H NMR (d_6DMSO, 400MHz) δ 9.21 (1H, m), 9.15 (1H, d, *J*=4.2 Hz), 8.83 (1H, s), 8.60 (1H, d, *J*=8.3Hz), 7.83 (1H, dd, *J*=8.3 and 4.2 Hz), 7.40-7.25 (4H, m), 7.15-7.00 (3H, m), 6.85 (1H, d, *J*=7.9Hz), 4.82 (2H, d, *J*=5.5Hz) ppm.
FAB MS calcd for $C_{22}H_{16}ClN_3O_3$ 406 (MH^+), found 406.
FAB HRMS exact mass calcd for $C_{22}H_{16}ClN_3O_3$ 406.09529 (MH^+), found 406.0944730.

EXAMPLE 30

Methyl (2R)-{[(8-hydroxy-1,6-naphthyridin-7-yl)carbonyl]amino} (phenyl)ethanoate



The title compound was prepared using the procedure described in Example 2, Step 2 replacing 2,5 dichlorobenzylamine with R(-)-2-phenylglycine methyl ester hydrochloride.

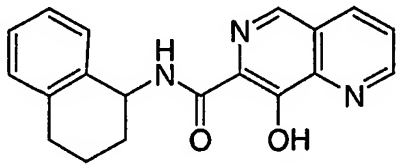
^{1}H NMR (d_6DMSO, 400MHz) δ 9.82 (1H, m), 9.17 (1H, d, *J*=4.2 Hz), 8.94 (1H, s), 8.64 (1H, d, *J*=8.2Hz), 7.85 (1H, ddd, *J*=8.2, 4.2 and 1.5 Hz), 7.60-7.30 (5H, m), 5.82 (1H, d, *J*=7.5 Hz), 3.72 (3H,s) ppm.

FAB MS calcd for $C_{18}H_{15}N_3O_4$ 338(MH^+), found 338.

FAB HRMS exact mass calcd for $C_{18}H_{15}N_3O_4$ 338.1135 (MH^+), found 338.1139.

EXAMPLE 31

8-hydroxy-N-(1,2,3,4-tetrahydronaphthalen-1-yl)-1,6-naphthyridine-7-carboxamide



The title compound was prepared using the procedure described in Example 2, Step 2 replacing 2,5 dichlorobenzylamine with 1,2,3,4 tetrahydro-1-napthylamine..

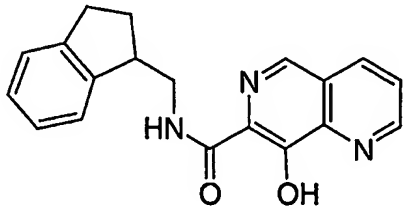
^{1}H NMR (d_6DMSO, 400MHz) δ 9.31(1H, d, *J*=9.1Hz), 9.17 (1H, d, *J*=4.3 Hz), 8.88 (1H, s), 8.61 (1H, d, *J*=8.3Hz), 7.84 (1H, dd, *J*=8.3 and 4.3 Hz), 7.30-7.00 (4H, m), 5.31 (1H, q, *J*=7.7 Hz), 3.00-2.60 (2H,m), 2.10-1.9 (3H,m), 1.85-1.70 (1H,m) ppm.

FAB MS calcd for $C_{19}H_{17}N_3O_2$ 320(MH^+), found 320.

FAB HRMS exact mass calcd for $C_{19}H_{17}N_3O_2$ 320.1394 (MH^+), found 320.1406.

EXAMPLE 32

N-(2,3-dihydro-1H-inden-1-ylmethyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide



The title compound was prepared using the procedure described in Example 2, Step 2 replacing 2,5 dichlorobenzylamine with 1-(2,3-dihydro-1H-inden-1-yl)methanamine.

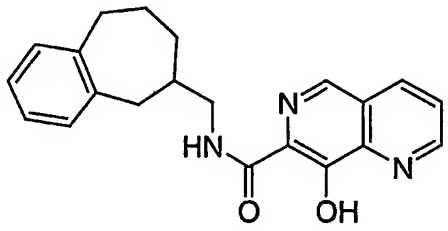
^{1}H NMR (d_6DMSO, 400MHz) δ 9.42 (1H, m), 9.17 (1H, d, *J*=4.1 Hz), 8.92 (1H, s), 8.61 (1H, d, *J*=8.3Hz), 7.84 (1H, dd, *J*=8.3 and 4.1 Hz), 7.40-7.10 (4H, m), 3.80-3.30 (3H,m), 3.05-2.70 (2H, m), 2.30-2.10 (1H, m) and 2.00-1.80 (1H, m) ppm.

FAB MS calcd for $C_{19}H_{17}N_3O_2$ 320(MH^+), found 320.

FAB HRMS exact mass calcd for $C_{19}H_{17}N_3O_2$ 320.1394 (MH^+), found 320.1393.

EXAMPLE 33

8-hydroxy-N-(6,7,8,9-tetrahydro-5H-benzo[a][7]annulen-6-ylmethyl)-1,6-naphthyridine-7-carboxamide



The title compound was prepared using the procedure described in Example 2, Step 2 replacing 2,5 dichlorobenzylamine with 1-(6,7,8,9-tetrahydro-5H-benzo[a][7]annulen-6-yl)methanamine.

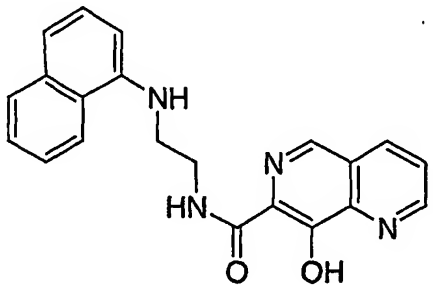
^{1}H NMR (d_6DMSO, 400MHz) δ 9.41 (1H, m), 9.16 (1H, dd, *J*=4.2 and 1.8Hz), 8.92 (1H, s), 8.61 (1H, dd, *J*=8.2 and 1.8Hz), 7.84 (1H, dd, *J*=8.2 and 4.2 Hz), 7.15-7.00 (4H, m), 3.40-3.20 (2H, m), 2.95-2.60 (4H, m), 2.00-1.75 (3H, m), 1.51 (1H, q, *J*=9.7Hz) and1.35(1H, q, *J*=9.7Hz) ppm.

FAB MS calcd for $C_{21}H_{21}N_3O_2$ 348 (MH^+), found 348.

FAB HRMS exact mass calcd for $C_{21}H_{21}N_3O_2$ 348.1707 (MH^+), found 348.1691.

EXAMPLE 34

8-hydroxy-N-[2-(1-naphthylamino)ethyl]-1,6-naphthyridine-7-carboxamide



The title compound was prepared using the procedure described in Example 2, Step 2 replacing 2,5 dichlorobenzylamine with N-(1-naphthyl)ethane-1,2-diamine..

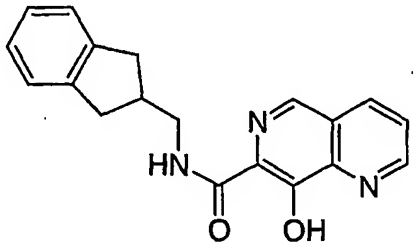
^1H NMR (d_6DMSO, 400MHz) δ 9.61 (1H, t, *J*=6.0 Hz), 9.17 (1H, d, *J*=4.2 Hz), 8.93 (1H, s), 8.62 (1H, d, *J*=8.3Hz), 8.15(1H, d, *J*=9.0 Hz), 7.84 (1H, dd, *J*=8.3 and 4.2 Hz), 7.77(1H, d, *J*=9.1 Hz), 7.50-7.35 (2H, m), 7.10 (2H, t, *J*=8.2Hz), 7.31 (1H, t, *J*=8.9Hz), 7.12(1H, d, *J*=8.2Hz), 6.70 (1H, d, *J*=7.7Hz), 3.74 (2H, q, *J*=6.2Hz), 3.47 (2H, t, *J*=6.6Hz) ppm.

FAB MS calcd for $C_{21}H_{18}N_4O_2$ 359 (MH^+), found 359.

FAB HRMS exact mass calcd for $C_{21}H_{18}N_4O_2$ 359.1503 (MH^+), found 359.1495.

EXAMPLE 35

N-(2,3-dihydro-1H-inden-2-ylmethyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide



The title compound was prepared using the procedure described in Example 2, Step 2 replacing 2,5 dichlorobenzylamine with 1-(2,3-dihydro-1H-inden-2-yl)methanamine

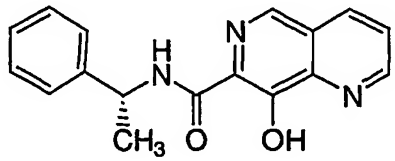
^{1}H NMR (d_6DMSO, 400MHz) δ 9.49 (1H, m), 9.17 (1H, d, *J*=4.2 Hz), 8.92 (1H, s), 8.61 (1H, d, *J*=8.4Hz), 7.84 (1H, dd, *J*=8.4 and 4.2 Hz), 7.25-7.15 (2H, m), 7.15-7.05 (2H, m), 3.44 (2H, t, *J*=6.6Hz), 3.10-2.95 (2H, m), 2.90-2.70 (3H, m) ppm.

FAB MS calcd for $C_{19}H_{17}N_3O_2$ 320 (MH^+), found 320.

FAB HRMS exact mass calcd for $C_{19}H_{17}N_3O_2$ 320.1394 (MH^+), found 320.1392.

EXAMPLE 36

8-hydroxy-N-[(1R)-1-phenylethyl]-1,6-naphthyridine-7-carboxamide



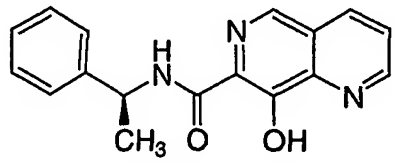
The title compound was prepared using the procedure described in Example 2, Step 2 replacing 2,5 dichlorobenzylamine with (R)-(+)-α-methylbenzylamine.

^{1}H NMR (DMSO-d6, 400MHz) δ 9.58 (1H, d, *J*=8.3Hz), 9.16 (1H, d, *J*=4.2Hz), 8.93 (1H, s), 8.62 (1H, d, *J*=8.3Hz), 7.84 (1H, dd, *J*=4.3 and 8.3Hz), 7.48 (2H, d, *J*=7.8Hz), 7.35 (2H, t, *J*=7.7), 7.25 (1H, t, *J*=7.4Hz), 5.26 (1H, m) and 1.60 (3H, d, *J*=7.0Hz)ppm.

FAB MS calcd for $C_{17}H_{15}N_3O_2$ 294.1 (MH^+), found 294.1.

EXAMPLE 37

8-hydroxy-N-[(1S)-1-phenylethyl]-1,6-naphthyridine-7-carboxamide



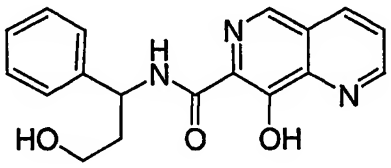
The title compound was prepared using the procedure described in Example 2, Step 2 replacing 2,5 dichlorobenzylamine with (S)-(-)-□□ -methylbenzylamine.

^{1}H NMR (DMSO-d6, 400MHz) δ 9.58 (1H, d, *J*=8.3Hz), 9.16 (1H, d, *J*=4.2Hz), 8.93 (1H, s), 8.62 (1H, d, *J*=8.3Hz), 7.84 (1H, dd, *J*=4.3 and 8.3Hz), 7.48 (2H, d, *J*=7.8Hz), 7.35 (2H, t, *J*=7.7), 7.25 (1H, t, *J*=7.4Hz), 5.26 (1H, m) and 1.60 (3H, d, *J*=7.0Hz)ppm.

FAB MS calcd for $C_{17}H_{15}N_3O_2$ 294.1 (MH^+), found 294.1.

EXAMPLE 38

8-hydroxy-N-(3-hydroxy-1-phenylpropyl)-1,6-naphthyridine-7-carboxamide



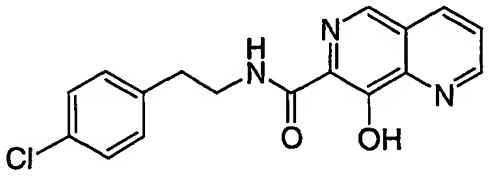
The title compound was prepared using the procedure described in Example 2, Step 2 replacing 2,5 dichlorobenzylamine with 3-amino-3-phenyl-1-propanol.

^{1}H NMR (DMSO-d6, 400MHz) δ 9.75 (1H, d, *J*=8.1Hz), 9.16 (1H, d, *J*=4.2Hz), 8.94 (1H, s), 8.61 (1H, d, *J*=8.3Hz), 7.83 (1H, dd, *J*=4.2 and 8.3Hz), 7.46 (2H, d, *J*=7.8Hz), 7.35 (2H, t, *J*=7.7Hz), 7.25 (1H, t, *J*=7.8Hz), 5.29 (1H, m), 3.45 (2H, t, *J*=5.8Hz), 2.20 (1H, m) and 2.05 (1H, m)ppm.

FAB MS calcd for $C_{18}H_{17}N_3O_3$ 324.1 (MH^+), found 324.1.

EXAMPLE 39

N-[2-(4-chlorophenyl)ethyl]-8-hydroxy-1,6-naphthyridine-7-carboxamide

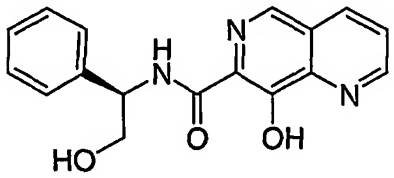


The title compound was prepared using the procedure described in Example 2, Step 2 replacing 2,5 dichlorobenzylamine with 4-chlorophenethylamine.

^{1}H NMR (DMSO-d6, 400MHz) δ 9.37 (1H, br s), 9.16 (1H, d, *J*=4.2Hz), 8.90 (1H, s), 8.61 (1H, d, *J*=8.3Hz), 7.83 (1H, dd, *J*=4.2 and 8.2Hz), 7.35 (2H, d, *J*=8.4Hz), 7.29 (2H, d, *J*=.8.4Hz), 3.61(2H, q, *J*=7Hz) and 2.93 (2H, t, *J*=7Hz)ppm.
FAB MS calcd for $C_{17}H_{14}ClN_3O_2$ 328.1 (MH^+), found 328.1.

EXAMPLE 40

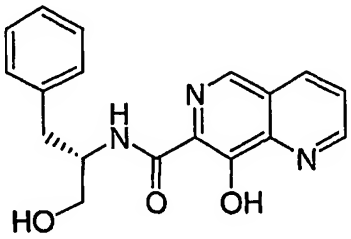
8-hydroxy-N-[(1R)-2-hydroxy-1-phenylethyl]-1,6-naphthyridine-7-carboxamide



The title compound was prepared using the procedure described in Example 2, Step 2 replacing 2,5 dichlorobenzylamine with (R)-(-)-2-phenyl glycinol.
^{1}H NMR (DMSO-d6, 400MHz) δ 9.49 (1H, d, 8Hz), 9.16 (1H, d, *J*=4.2Hz), 8.96 (1H, s), 8.64 (1H, d, *J*=8.3Hz), 7.85 (1H, dd, *J*=4.2 and 8.2Hz), 7.45 (2H, d, *J*=8.4Hz), 7.35 (2H, t, *J*=.7Hz), 7.26(1H, t, *J*=7Hz), 5.13 (1H, m), 3.88(1H, dd, *J*=7.5 and 11Hz) and 3.78 (1H, dd, *J*=5.6 and 11Hz)ppm.
FAB MS calcd for $C_{17}H_{15}N_3O_3$ 310.1 (MH^+), found 310.1.

EXAMPLE 41

N-[(1S)-1-benzyl-2-hydroxyethyl]-8-hydroxy-1,6-naphthyridine-7-carboxamide



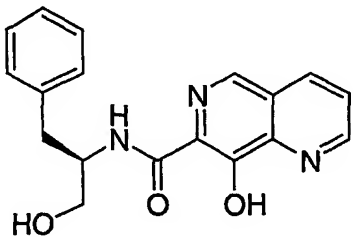
The title compound was prepared using the procedure described in Example 2, Step 2 replacing 2,5 dichlorobenzylamine with (S)-(-)-2-amino-3-phenyl-1-glycinol.
^{1}H NMR (DMSO-d6, 400MHz) δ 13.7 (1H, s), 9.15 (1H, d, *J*=4.2Hz), 8.96 (1H, d, *J*=8.2Hz), 8.91 (1H, s), 8.60 (1H, d, *J*=8.3Hz), 7.83 (1H, dd, *J*=4.2 and 8.2Hz), 7.26

(4H, m), 7.16(1H, m), 5.02 (1H, br s), 4.28 (1H, m), 3.55 (2H, br s) and 2.96 (2H, m)ppm.

FAB MS calcd for $C_{18}H_{17}N_3O_3$ 324.1 (MH^+), found 324.1.

EXAMPLE 42

N-[(1R)-1-benzyl-2-hydroxyethyl]-8-hydroxy-1,6-naphthyridine-7-carboxamide



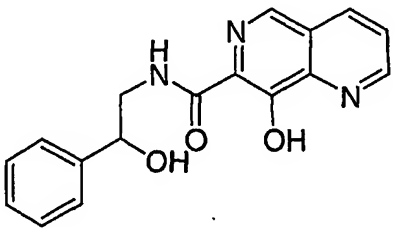
The title compound was prepared using the procedure described in Example 2, Step 2 replacing 2,5 dichlorobenzylamine with (R)-(+)-2-amino-3-phenyl-1-glycinol.

^{1}H NMR (DMSO-d6, 400MHz) δ 13.7 (1H, s), 9.15 (1H, d, *J*=4.2Hz), 8.96 (1H, d, *J*=8.2Hz), 8.91 (1H, s), 8.60 (1H, d, *J*=8.3Hz), 7.83 (1H, dd, *J*=4.2 and 8.2Hz), 7.26 (4H, m), 7.16(1H, m), 5.02 (1H, br s), 4.28 (1H, m), 3.55 (2H, br s) and 2.96 (2H, m)ppm.

FAB MS calcd for $C_{18}H_{17}N_3O_3$ 324.1 (MH^+), found 324.1.

EXAMPLE 43

8-hydroxy-N-(2-hydroxy-2-phenylethyl)-1,6-naphthyridine-7-carboxamide



The title compound was prepared using the procedure described in Example 2, Step 2 replacing 2,5 dichlorobenzylamine with 2-amino-1-phenylethanol.

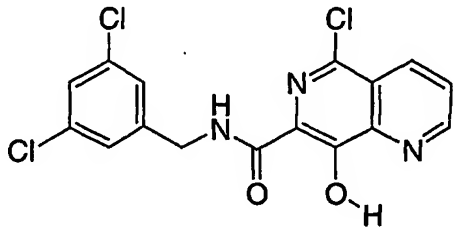
^{1}H NMR (DMSO-d6, 400MHz) δ 9.17 (1H, d, *J*=4.2Hz), 9.08 (1H, br s), 8.91 (1H, s), 8.61 (1H, d, *J*=8.4Hz), 7.84 (1H, dd, *J*=4.4 and 8.2Hz), 7.42 (2H, d, *J*=7.2Hz),

7.35 (2H, t, *J*=7.4Hz), 7.26 (1H, t, *J*=7.2Hz), 4.88 (1H, dd, *J*=4.6 and 8.1Hz), 3.4-3.7 (2H, m)ppm.

FAB MS calcd for $C_{17}H_{15}N_3O_3$ 310.1 (MH^+), found 310.1.

EXAMPLE 44

5-chloro-N-(3,5-dichlorobenzyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide



Step 1: Preparation of Methyl-N-{[2-(isopropoxycarbonyl)pyridin-3-yl]carbonyl}glycine

A solution of isopropyl 3-(chlorocarbonyl)pyridine-2-carboxylate (prepared as in P. Ornstein et. al. *J. Med. Chem.* 1989, 32, 827) (6.577g, 31.44 mmol) in CH_2Cl_2 (50 ml) was added dropwise to a solution of glycine methyl ester hydrochloride (4.34g, 34.58 mmol) and diisopropylethylamine (12.6 ml, 72.31 mmol) in CH_2Cl_2 (65ml) at 0C. The reaction was stirred for 16 hrs during which time the ice bath was allowed to expire. The solvent was evaporated in vacuo and the residue was used in the next step without further purification.

FAB MS calcd for $C_{13}H_{16}N_2O_5$ 281 (MH^+), found 281.

Step 2: Preparation of methyl 5,8-dihydroxy-1,6-naphthyridine-7-carboxylate

The crude product from Step 1 (31.44 mmol) was dissolved in methanol (288 ml) and treated with sodium methoxide (28.7 ml of a 4.373M solution in methanol, 125.8 mmol) and heated at reflux for 16 hrs The reaction was cooled to room temperature and neutralized to pH 7 with aq. HCl and the solvent was evaporated in vacuo. The residue was partitioned between water and $CHCl_3$ and the organic layer separated and dried (Na_2SO_4). The solvent was evaporated in vacuo to afford the title compound along with its regioisomer, which were used in the next step without further purification.

FAB MS calcd for $C_{10}H_8N_2O_4$ 221 (MH^+), found 221.

Step 3: Preparation of methyl 5-chloro-8-hydroxy-1,6-naphthyridine-7-carboxylate

The crude material from Step 2 (5.47g, 24.85 mmol) was suspended in phosphorous oxychloride (45 ml) and heated at 106C for 30 mins. The solvent was evaporated in vacuo and the residue was cooled to 0C and treated sequentially with methanol (45mL0 and then with a solution of sodium methoxide until a pH of >12 was obtained. The reaction was stirred for 2 hrs and then neutralised to pH 7 with sat. aq. NH_4Cl. The methanol was evaporated in vacuo and the residue was extracted with CH_2Cl_2 and dried (Na_2SO_4). The solvent was evaporated in vacuo to afford the title compound along with its regioisomer, which were used in the next step without further purification.

FAB MS calcd for $C_{10}H_7ClN_2O_3$ 239 (MH^+), found 239.

Step 4: Preparation of Methyl 5-chloro-8-[(4-methoxybenzyl)oxy]-1,6-naphthyridine-7-carboxylate

To a slurry of the phenol from Step 3 (7.379g, 30.79 mmol and cesium carbonate (11.04g, 33.87 mmol) in DMF (154 ml) was added 4 methoxybenzyl chloride (4.38 ml, 32.33 mmol) at rom temperature and the reaction was then warmed to 50C and stirred at this temperature for 16hrs. The reaction mixture was ppoured into water and extracted into EtOAc and dried (Na_2SO_4).The solvent was evaporated in vacuo and the residue was chromatographed (SiO2, gradient elution, 25-30% EtOAc in hexanes) to afford a solid, which was washed with hexanes and then diethyl ether and dried in vacuo to afford the title compound.

FAB MS calcd for $C_{10}H_7ClN_2O_3$ 359 (MH^+), found 359.

Step 5: Preparation of 5-chloro-N-(3,5-dichlorobenzyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide

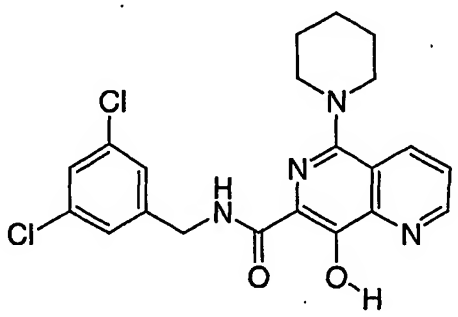
The title compound was prepared using the procedure described in Example 1, Step 3 replacing with methyl 8-hydroxy-1,6-naphthyridine-7-carboxylate with methyl 5-chloro-8-[(4-methoxybenzyl)oxy]-1,6-naphthyridine-7-carboxylate from Step 4..

^1H NMR ($CDCl_3$, 400MHz) δ 13.13 (1H, s), 9.25 (1H, d, *J*=4.2Hz), 8.61 (1H,d, *J*=8.5 Hz), 8.23 (1H, brs), 7.77 (1H, dd, *J*=8.5 and 4.2 Hz), 7.35-7.20 (3H, m), 4.65 (2H, d, *J*=6.4 Hz) ppm.

FAB MS calcd for $C_{16}H_{10}N_3O_2Cl_3$ 383 (MH^+), found 383.

EXAMPLE 45

N-(3,5-dichlorobenzyl)-8-hydroxy-5-piperidin-1-yl-1,6-naphthyridine-7-carboxamide



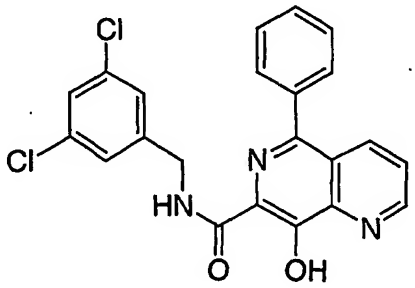
A solution of the chloride from Example 44 Step 5 (40 mg, 0.105 mmol) in piperidine (0.5ml) was heated at 100C for 36 hrs under argon. The resulting solution was cooled to room temperature and the solvent evaporated in vacuo.The residue was dissolved in hot DMF (0.7 ml) and purified by preparative HPLC. (Gilson semi preparative HPLC system and a YMC Combiprep Pro Column (50X20mm I.D., C18, S-5 um, 120A) eluting with 5 - 95% acetonitrile/water (0.1% TFA) at 15 ml/min) to afford the title compound after lyophilization.

^1H NMR ($CDCl_3$, 400MHz) δ 9.30 (1H, s), 8.60 (1H, d, J=8.6 Hz), 8.24 (1H, brs), 7.74 (1H, m), 7.35-7.20 (3H, m), 4.65 (2H, d, J=6.2 Hz), 3.26 (4H,m), 1.84 (4H,m) and 1.71 (2H, m) ppm.

FAB MS calcd for $C_{21}H_{20}N_4O_2Cl_2$ 431 (MH^+), found 431.

EXAMPLE 46

N-(3,5-dichlorobenzyl)-8-hydroxy-5-phenyl-1,6-naphthyridine-7-carboxamide



Step 1: Preparation of methyl 8-[(4-methoxybenzyl)oxy]-5-phenyl-1,6-naphthyridine-7-carboxylate

A solution of the chloride from Example 44 Step 4 (100 mg, 0.279 mmol), phenyl boronic acid (37.4 mg, 0.307 mmol), tetrakis triphenylphosphine palladium (32.24 mg, 0.0279 mmol) and potassium carbonate (88.95 mg, 0.419 mmol) in DMF (1.7 ml) was stirred at 100C for 16 hrs. The reaction was allowed to cool to room temperature and pored into water and extracted into CH_2Cl_2 and dried (Na_2SO_4). The solvent was evaporated *in vacuo* and the residue was chromatographed (SiO_2, gradient elution, 20-30% EtOAc in hexanes) to afford the title compound.

FAB MS calcd for $C_{24}H_{20}N_2O_4$ 401 (MH^+), found 401.

Step 2: Preparation of N-(3,5-dichlorobenzyl)-8-hydroxy-5-phenyl-1,6-naphthyridine-7-carboxamide

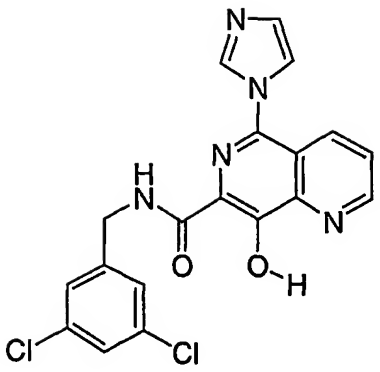
A mixture of the ester from Step 1 (40 mg, 0.10 mmol) and 3,5,dichlorobenzylamine (0.35 g, 2.0 mmol) were heated at 100C for 18hrs. The solvent was evaporated *in vacuo* and the residue was purified by preparative HPLC. (Gilson semi preparative HPLC system and a YMC Combiprep Pro Column (50X20mm I.D., C18, S-5 um, 120A) eluting with 5 - 95% acetonitrile/water (0.1% TFA) at 15 ml/min) to afford the title compound after lyophilization. .

^1H NMR ($CDCl_3$, 400MHz) δ 9.23 (1H, d, *J*=4.2 Hz), 8.53 (1H, m), 8.42 (1H, d, *J*=8.6Hz), 7.70-7.45 (6H, m), 7.30-7.10 (3H, m), 4.66 (2H, d, *J*=5.4 Hz) ppm.

FAB MS calcd for $C_{22}H_{15}N_3O_2Cl_2$ 424 (MH^+), found 424.

EXAMPLE 47

N-(3,5-dichlorobenzyl)-8-hydroxy-5-(1H-imidazol-1-yl)-1,6-naphthyridine-7-carboxamide



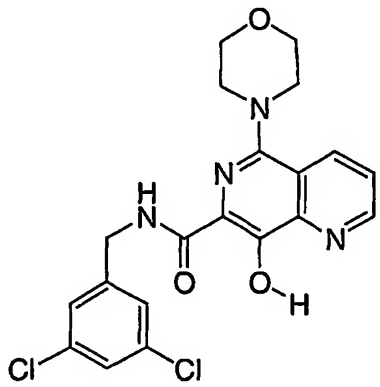
The chloride from Example 44 Step 5 (8.0 mg, 0.021 mmol) and imidazole (80mg) were fused at 160C for 1 hr under argon. The residue was dissolved in DMF (0.5 ml) and purified by preparative HPLC. (Gilson semi preparative HPLC system and a YMC Combiprep Pro Column (50X20mm I.D., C18, S-5 um, 120A) eluting with 5 - 95% acetonitrile/water (0.1% TFA) at 15 ml/min) to afford the title compound after lyophilization.

^{1}H NMR ($CDCl_3$, 400MHz) δ 9.27 (1H, d, *J*=4.2 Hz), 8.23 (1H, d, *J*=7.5 Hz), 7.96 (1H, s), 7.73 (1H, dd, *J*=4.2 and 8.6 Hz), 7.40 (1H, s), 7.38-7.20 (3H, m), 4.66 (2H, d, *J*=6.2 Hz) ppm.

FAB MS calcd for $C_{19}H_{13}N_5O_2Cl_2$ 414 (MH^+), found 414.

EXAMPLE 48

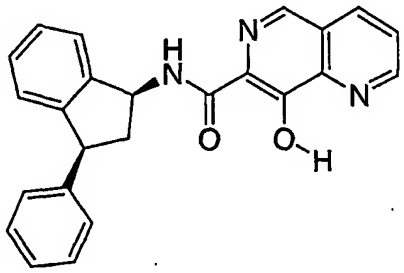
N-(3,5-dichlorobenzyl)-8-hydroxy-5-morpholin-4-yl-1,6-naphthyridine-7-carboxamide



A solution of the chloride from Example 44 Step 5 (14 mg, 0.037 mmol) in morpholine (0.5ml) was heated at 120C for 36 hrs under argon. The resulting solution was cooled to room temperature and the solvent evaporated in vacuo.The residue was dissolved in hot DMF (0.5 ml) and purified by preparative HPLC. (Gilson semi preparative HPLC system and a YMC Combiprep Pro Column (50X20mm I.D., C18, S-5 um, 120A) eluting with 5 - 95% acetonitrile/water (0.1% TFA) at 15 ml/min) to afford the title compound after lyophilization.
^{1}H NMR ($CDCl_3$, 400MHz) δ 9.24 (1H, d, *J*=4.4 Hz), 8.60 (1H, d, *J*=8.2 Hz), 8.20 (1H, brs), 7.68 (1H, dd, *J*=4.4 and 8.2Hz), 7.35-7.20 (3H, m), 4.67 (2H, d, *J*=6.3 Hz), 3.98 (4H, t, *J*=4.5Hz), and 3.28 (4H, t, *J*=4.5Hz) ppm.
FAB MS calcd for $C_{20}H_{18}N_4O_3Cl_2$ 433 (MH^+), found 433.

EXAMPLE 49

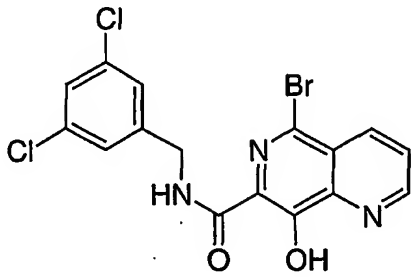
8-hydroxy-N-[(cis)-3-phenyl-2,3-dihydro-1H-inden-1-yl]-1,6-naphthyridine-7-carboxamide



The title compound was prepared using the procedure described in Example 2, Step 2 replacing 2,5 dichlorobenzylamine with cis-3-phenyl-2,3-dihydro-1H-inden-1-amine (Baltrop et al *J. Chem. Soc.* 1956, 2928).
^{1}H NMR ($CDCl_3$, 400MHz) δ 9.22 (1H, d, *J*=4.2 Hz), 8.65 (1H, s), 8.41(1H, d, *J*=9.3 Hz), 8.31 (1H, d, *J*=8.4Hz), 7.68 (1H, dd, *J*=4.2 and 8.4Hz),7.41 (1H, d, *J*=7.0Hz), 7.38-7.20 (7H, m), 6.98 (1H, d, *J*=7.7Hz), 5.76 (1H, q, *J*=8.4Hz), 4.35 (1H, t, *J*=7.2Hz), 3.17 (1H, dt, *J*=12.6 and 7.3Hz), 2.04(1H, dt, *J*=12.6 and 9.7Hz) ppm.
FAB MS calcd for $C_{24}H_{19}N_3O_2$ 382 (MH^+), found 382.

EXAMPLE 50

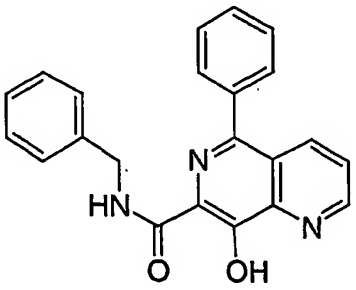
5-bromo-N-(3,5-dichlorobenzyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide



To a solution of N-(3,5-dichlorobenzyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide from Example 1, Step 3 (1.28g, 3.69 mmol) in CH_2Cl_2 (100 ml) at room temperature was added N-bromosuccinimide (0.689g, 3.87 mmol). The reaction was stirred for 4hrs and then poured into water. The organic phase was washed with water (3x 100ml), and dried (Na_2SO_4). The solvent was evaporated *in vacuo* and the residue triturated with CH_2Cl_2 to afford the title compound as an off white solid.
^1H NMR ($CDCl_3$, 400MHz) δ 13.12 (1H, s), 9.21 (1H, d, *J*=4.4 Hz), 8.60 (1H, d, *J*=8.4 Hz), 8.23 (1H, brs), 7.75 (1H, dd, *J*=4.2 and 8.4Hz), 7.35-7.20 (3H, m), 4.66 (2H, d, *J*=6.4 Hz) ppm.
FAB MS calcd for $C_{16}H_{10}Br\ Cl_2N_3O_2$ 426 (MH^+), found 426.

EXAMPLE 51

N-(benzyl)-8-hydroxy-5-phenyl-1,6-naphthyridine-7-carboxamide



A mixture of the ester from Example 44 Step 1 (21 mg, 0.0524 mmol) and benzylamine (0.0.143ml, 1.31 mmol) were heated at 100C for 18hrs. The reaction was diluted with DMF (0.4ml) and purified by preparative HPLC. (Gilson semi preparative HPLC system and a YMC Combiprep Pro Column (50X20mm I.D., C18,

S-5 um, 120A) eluting with 5 - 95% acetonitrile/water (0.1% TFA) at 15 ml/min) to afford the title compound after lyophilization. .

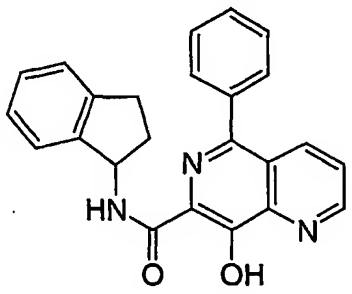
^{1}H NMR ($CDCl_3$, 400MHz) δ 9.20 (1H, d, *J*=4.0 Hz), 8.53 (1H, m), 8.42 (1H, dd, *J*=8.6 and 2.5 Hz), 7.70-7.45 (6H, m), 7.45-7.15 (5H, m), 4.66 (2H, d, *J*=6.5 Hz) ppm.

FAB MS calcd for $C_{22}H_{17}N_3O_2$ 356 (MH^+), found 356.

FAB HRMS exact mass calcd for $C_{22}H_{17}N_3O_2$ 356.1393533 (MH^+), found 356.1386040.

EXAMPLE 52

N-(2,3-dihydro-1H-inden-1-yl)-8-hydroxy-5-phenyl-1,6-naphthyridine-7-carboxamide



The title compound was prepared using the procedure described in Example 51 replacing benzylamine with aminoindane.

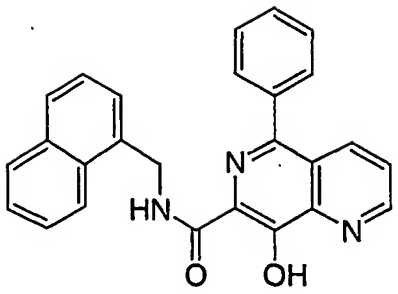
^{1}H NMR ($CDCl_3$, 400MHz) δ 9.23 (1H, d, *J*=4.0 Hz), 8.44 (1H, d, *J*=1.5Hz), 8.42 (1H, dd, *J*=8.4, 1.5 Hz), 8.34 (1H, d, *J*=8.7 Hz), 7.62 (1H, dd, *J*=8.4 and 4.2Hz), 7.60-7.45 (4H, m), 7.38 (1H, d, *J*=7.5 Hz), 7.35-7.15 (5H, m), 5.75 (1H, q, *J*=8.0Hz), 3.20-2.90 (2H, m), 2.73 1H, m) and 2.20-1.80 (1H, m) ppm.

FAB MS calcd for $C_{24}H_{20}N_3O_2$ 382 (MH^+), found 382.

FAB HRMS exact mass calcd for $C_{24}H_{20}N_3O_2$ 382.1550033 (MH^+), found 382.1549400.

EXAMPLE 53

8-hydroxy-N-(1-naphthylmethyl)-5-phenyl-1,6-naphthyridine-7-carboxamide



The title compound was prepared using the procedure described in Example 51 replacing benzylamine with 1-napthylmethylamine.

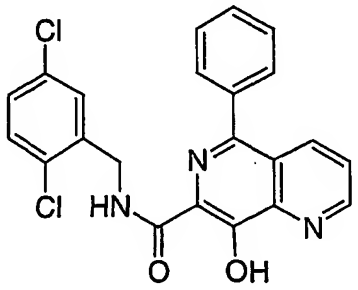
^{1}H NMR ($CDCl_3$, 400MHz) δ 9.20 (1H, d, *J*=4.0 Hz), 8.44 (1H, m), 8.37 (1H, dd, *J*=8.4 and 1.7 Hz), 8.15 (1H, d, *J*=8.3 Hz), 7.89 (1H, d, *J*=7.8 Hz), 7.84 (1H, d, *J*=8.1 Hz), 7.60-7.00 (10H, m), 5.18 (1H, d, *J*=6.2Hz) ppm.

FAB MS calcd for $C_{26}H_{19}N_3O_2$ 406 (MH^+), found 406.

FAB HRMS exact mass calcd for $C_{26}H_{19}N_3O_2$ 406.1550033 (MH^+), found 406.1562180.

EXAMPLE 54

N-(2,5-dichlorobenzyl)-8-hydroxy-5-phenyl-1,6-naphthyridine-7-carboxamide



The title compound was prepared using the procedure described in Example 51 replacing benzylamine with 2,5-dichlorobenzylamine.

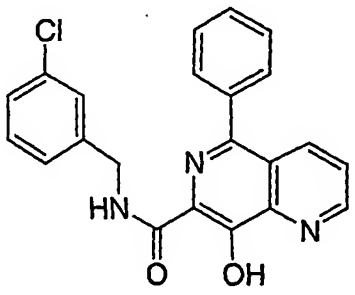
^{1}H NMR ($CDCl_3$, 400MHz) δ 9.20 (1H, d, *J*=4.0 Hz), 8.62 (1H, m), 8.42 (1H, dd, *J*=8.6, 2.5 Hz), 7.70-7.20 (9H, m), 4.76 (2H, d, *J*=7.6 Hz) ppm.

FAB MS calcd for $C_{22}H_{15}Cl_2N_3O_2$ 424 (MH^+), found 424.

FAB HRMS exact mass calcd for $C_{22}H_{15}Cl_2N_3O_2$ 424.0614086 (MH^+), found 424.0616930.

EXAMPLE 55

N-(3-chlorobenzyl)-8-hydroxy-5-phenyl-1,6-naphthyridine-7-carboxamide



The title compound was prepared using the procedure described in Example 51 replacing benzylamine with 3-chlorobenzylamine.

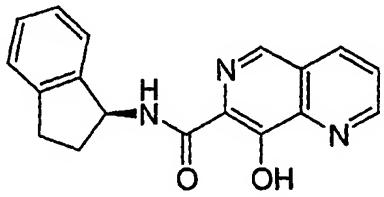
^{1}H NMR ($CDCl_3$, 400MHz) δ 9.23 (1H, d, *J*=2.7 Hz), 8.52 (1H, m), 8.44 (1H, dd, *J*=8.8 and 1.5 Hz), 7.70-7.20 (10H, m), 4.68 (2H, d, *J*=6.6 Hz) ppm.

FAB MS calcd for $C_{22}H_{16}Cl\ N_3O_2$ 390 (MH^+), found 390.

FAB HRMS exact mass calcd for $C_{22}H_{16}Cl\ N_3O_2$ 390.1003809 (MH^+), found 390.1008681.

EXAMPLE 56

N-[(1S)-2,3-dihydro-1H-inden-1-yl]-8-hydroxy-1,6-naphthyridine-7-carboxamide



The title compound was prepared using the procedure described in Example 2, Step 2 replacing 2,5 dichlorobenzylamine with 1(S) aminoindane.

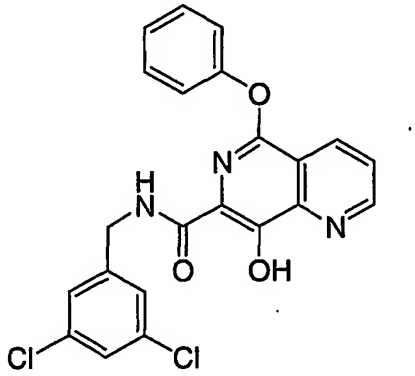
^{1}H NMR (d_6DMSO, 400MHz) δ 9.41 (1H, d, *J*=8.2Hz), 9.18 (1H, d, *J*=4.2 Hz), 8.90 (1H, s), 8.63 (1H, d, *J*=8.2Hz), 7.85 (1H, dd, *J*=8.2 and 4.2 Hz), 7.35-7.10 (4H, m), 5.63 (1H, q, *J*=8.2 Hz), 3.20-2.80 (2H, m), 2.60-2.40 (1H, m), 2.30-2.10 (1H, m) ppm.

FAB MS calcd for $C_{18}H_{15}N_3O_2$ 306 (MH^+), found 306.

FAB HRMS exact mass calcd for $C_{18}H_{15}N_3O_2$ 306.1237 (MH^+), found 306.1209

EXAMPLE 57

N-(3,5-dichlorobenzyl)-8-hydroxy-5-phenoxy-1,6-naphthyridine-7-carboxamide

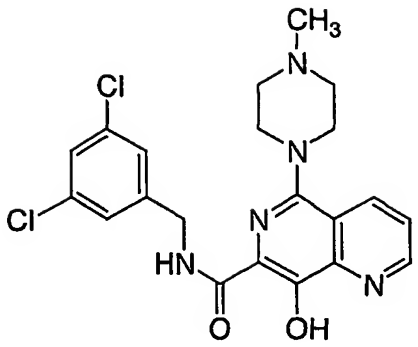


To a solution of 5-bromo-N-(3,5-dichlorobenzyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide from Example 50 (26 mg, 0.068 mmol), phenol (28mg, 0.304 mmol) and cesium carbonate (198 mg, 0.608 mmol) in DMPU (0.25 ml) was heated at 140C for 8 hrs. The reaction was poured into sat aq. Na_2CO_3 and extracted with $CHCl_3$. The organic phase was washed with water and dried (Na_2SO_4). The solvent was evaporated *in vacuo* and the residue dissolved in DMF (0.7ml) and purified by preparative HPLC. (Gilson semi preparative HPLC system and a YMC Combiprep Pro Column (50X20mm I.D., C18, S-5 um, 120A) eluting with 5 - 95% acetonitrile/water (0.1% TFA) at 15 ml/min) to afford the title compound after lyophilization.

^1H NMR ($CDCl_3$, 400MHz) δ 12.55 (1H, s), 9.31 (1H, d, J=4.4 Hz), 8.80 (1H, d, J=8.4 Hz), 7.78 (1H, dd, J=4.4and 8.4Hz), 7.61(1H, t, J=5.5 Hz), 7.44 (2H, t, J=7.9 Hz), 7.35-7.20 (6H, m), 7.10 (2H, d, J=1.8Hz), 4.49 (2H, d, J=6.2 Hz) ppm.
FAB MS calcd for $C_{22}H_{15}Cl_2N_3O_3$ 440 (MH^+), found 440.

EXAMPLE 58

N-(3,5-dichlorobenzyl)-8-hydroxy-5-(4-methylpiperazin-1-yl)-1,6-naphthyridine-7-carboxamide



To a solution of 5-bromo-N-(3,5-dichlorobenzyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide from Example 50 (25 mg, 0.060 mmol), N-methyl piperazine (35.2 mg, 0.35 mmol) in DMF (0.25 ml) was heated at 135C for 48 hrs. The reaction mixture was diluted with DMF (0.25 ml) and purified by preparative HPLC. (Gilson semi preparative HPLC system and a YMC Combiprep Pro Column (50X20mm I.D., C18, S-5 um, 120A) eluting with 5 - 95% acetonitrile/water (0.1% TFA) at 15 ml/min) to afford the title compound after lyophilization.

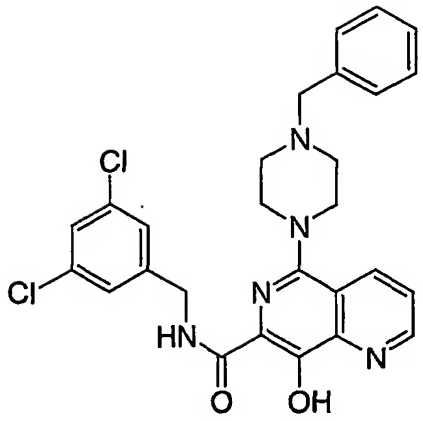
^{1}H NMR ($CDCl_3$, 400MHz) δ 13.0 (1H, s), 9.21 (1H, d, *J*=4.2 Hz), 8.36 (1H, dd, *J*=8.4 and 1.5 Hz), 8.25 (1, t, *J*=6.4 Hz), 7.65 (1H, dd, *J*=4.2 and 8.4Hz), 7.35-7.20 (3H, m), 4.67 (2H, d, *J*=6.2 Hz), 3.79 (2H, d, *J*=11.9 Hz), 3.60 (4H, m), 3.19 (2H, m) and 2.96 (3H, s) ppm.

FAB MS calcd for $C_{21}H_{21}Cl_2N_5O_3$ 446 (MH^+), found 446.

FAB HRMS exact mass calc'd for $C_{21}H_{21}Cl_2N_5O_3$ 446.1145 (MH^+), found 446.1138.

EXAMPLE 59

5-(4-benzylpiperazin-1-yl)-N-(3,5-dichlorobenzyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide



The title compound was prepared using the procedure described in Example 58 replacing N–methyl piperazine with N-benzylpiperazine.

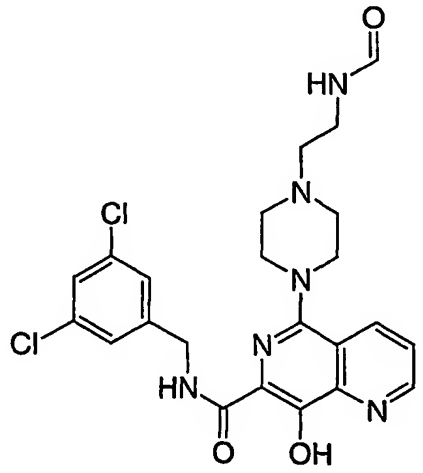
^{1}H NMR ($CDCl_3$, 400MHz) δ 12.94 (1H, s), 9.21 (1H, dd, *J*=4.3 and 1.5 Hz), 8.33 (1H, dd, *J*=8.4 and 1.6 Hz), 8.27(1H, t, *J*=6.4 Hz), 7.62 (1H, dd, *J*=4.2 and 8.4Hz), 7.55-7.40 (5H, m), 7.35-7.20 (3H, m),4.64 (2H, d, *J*=6.6Hz), 4.32 (2H, s), 3.80-3.50 (6H, m), 3.12 (2H ,t, *J*=9.0 Hz) ppm.

FAB MS calcd for $C_{27}H_{25}Cl_2N_5O_2$ 522 (MH^+), found 522.

FAB HRMS exact mass calc'd for $C_{27}H_{25}Cl_2N_5O_2$ 522.1458 (MH^+), found 522.1420.

EXAMPLE 60

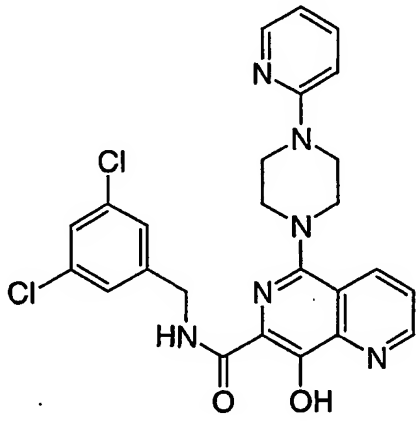
N-(3,5-dichlorobenzyl)-5-{4-[2-(formylamino)ethyl]piperazin-1-yl}-8-hydroxy-1,6-naphthyridine-7-carboxamide



The title compound was prepared using the procedure described in Example 58 replacing N–methyl piperazine with 2-piperazin-1-ylethanamine.
^{1}H NMR ($CDCl_3$, 400MHz) δ 12.99 (1H, s), 9.20 (1H, dd, *J*=4.2 and 1.6 Hz), 8.35 (1H, dd, *J*=8.4 and 1.6 Hz), 8.22 (1H, s), 7.82 (1H, t, *J*=6.0 Hz), 7.64 (1H, dd, *J*=4.2 and 8.4Hz), 7.35-7.40 (3H, m), 4.66 (2H, d, *J*=6.6Hz), 4.00-3.10 (12H, m) ppm.
FAB MS calcd for $C_{23}H_{24}Cl_2N_6O_3$ 503 (MH^+), found 503.
FAB HRMS exact mass calc'd for $C_{23}H_{24}Cl_2N_6O_3$ 503.1360 (MH^+), found 503.1371.

EXAMPLE 61

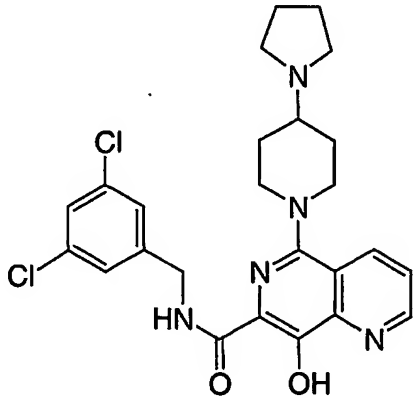
N-(3,5-dichlorobenzyl)-8-hydroxy-5-(4-pyridin-2-ylpiperazin-1-yl)-1,6-naphthyridine-7-carboxamide



The title compound was prepared using the procedure described in Example 58 replacing N–methyl piperazine with N-pyridin-2-ylpiperazine.
^{1}H NMR ($CDCl_3$, 400MHz) δ 12.87 (1H, s), 9.20 (1H, dd, *J*=4.4 and 1.6 Hz), 8.46 (1H, dd, *J*=8.5 and 1.6 Hz), 8.29 (1H, t, *J*=6.6 Hz), 7.26 (1H, dd, *J*=6.1 and 1.8Hz), 7.89 (1H,m), 7.66 (1H, dd, J=4.4 and 8.5 Hz), 7.35-7.20 (3H, m), 7.04 (1H, d, *J*=9.1Hz), 6.92 (1H, t, J=6.5 Hz), 4.66 (2H, d, *J*=6.4Hz), 4.02 (4H, t, *J*=5.0Hz), 3.50 (4H, t, *J*=5.0Hz) ppm.
FAB MS calcd for $C_{25}H_{22}Cl_2N_6O_3$ 509 (MH^+), found 509.
FAB HRMS exact mass calc'd for $C_{25}H_{22}Cl_2N_6O_3$ 509.1254 (MH^+), found 509.1257.

EXAMPLE 62

N-(3,5-dichlorobenzyl)-8-hydroxy-5-(4-pyrrolidin-1-ylpiperidin-1-yl)-1,6-naphthyridine-7-carboxamide



The title compound was prepared using the procedure described in Example 58 replacing N–methyl piperazine with 4-pyrrolidin-1-ylpiperidine.
^{1}H NMR ($CDCl_3$, 400MHz) δ 12.75 (1H, s), 9.20 (1H, dd, *J*=4.2 and 1.6 Hz), 8.41 (1H, dd, *J*=8.4 and 1.6 Hz), 8.15 (1H, t, *J*=6.4 Hz), 7.64 (1H, dd, *J*=4.2 and 8.4Hz), 7.35-7.20 (3H, m), 4.66 (2H, d, *J*=6.4Hz), 3.94 (2H, m), 3.70(2H, m) 3.12 (1H, m), 3.00-2.80(2H,m), 2.40-1.80 (8H, m)ppm.
FAB MS calcd for $C_{25}H_{27}Cl_2N_5O_2$ 500 (MH^+), found 500.
FAB HRMS exact mass calc'd for $C_{25}H_{27}Cl_2N_5O_2$ 500.1615 (MH^+), found 500.1626.

EXAMPLE 63

5-anilino-N-(3,5-dichlorobenzyl)-8-hydroxy-1,6-naphthyridine-7-carboxamide